1616

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TRANSMITTAL FORM

(to be used for all correspondence after initial filing)

Application Number	09/721,131
Filing Date	November 22, 2000
First Named Inventor	Bass, Ralph L.
Group Art Unit	1616
Examiner Name	Frank Choi
Total Number of Pages in This Submission	71
Attorney Docket Number	014123-000008

ENCLOSURES (check all that apply)

- [X] Fee Transmittal Form
- [X] Fee Attached
- [ ] Amendment / Reply
- [ ] After Final
- [ ] Affidavits/declaration(s)
- [ ] Extension of Time Request
- [ ] Express Abandonment Request
- [ ] Information Disclosure Statement
- [ ] Certified Copy of Priority Documents
- [ ] Response to Missing Parts/ Incomplete Application
- [ ] Response to Missing Parts under 37 CFR 1.52 or 1.53
- [ ] Assignment Papers *(for an Application)*
- [ ] Drawing(s)
- [ ] Licensing-related Papers
- [ ] Petition
- [ ] Petition to Convert to a Provisional Application
- [ ] Power of Attorney, Revocation Change of Correspondence Address
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- [ ] After Allowance Communication to Group
- [ ] Appeal Communication to Board of Appeals and Interferences
- [X] Appeal Communication to Group *(Appeal Notice, Brief, Reply Brief)*
- [ ] Proprietary Information
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- [X] Other Enclosure(s) *(please identify below):* **Check in the amount of $160; acknowledgement postcard**

Remarks

SIGNATURE OF APPLICANT, ATTORNEY, OR AGENT

Firm or Individual Name	MOORE & VAN ALLEN JENNIFER L. SKORD, REG. NO. 30,687
Signature	Jennifer L. Skord
Date	April 21, 2003

CERTIFICATE OF MAILING

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FEE TRANSMITTAL for FY 2003

Patent fees are subject to annual revision.

TOTAL AMOUNT OF PAYMENT	($) 160.00

Complete if Known	
Application Number	09/721,131
Filing Date	November 22, 2000
First Named Inventor	Bass, Ralph L.
Examiner Name	Frank Choi
Group Art Unit	1616
Attorney Docket No.	014123-000008

METHOD OF PAYMENT *(check all that apply)*

☒ Check ☐ Credit Card ☐ Money Order ☐ Other ☐ None

☒ Deposit Account:

Deposit Account Number: 13-4365

Deposit Account Name: MOORE & VAN ALLEN PLLC

The Commisioner is authorized to: *(check all that apply)*

☐ Charge fee(s) indicated below ☒ Credit any overpayments

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FEE CALCULATION

1. BASIC FILING FEE

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
101	750	201	375	Utility filing fee	
106	330	206	165	Design filing fee	
107	520	207	260	Plant filing fee	
108	750	208	375	Reissue filing fee	
114	160	214	80	Provisional filing fee	

SUBTOTAL(1) ($) 0.00

2. EXTRA CLAIM FEES FOR UTILITY AND REISSUE

			Extra Claims		Fee from below		Fee Paid
Total Claims		-20**=		X		=	
Independent		-3**=		X		=	
Claims						=	
Multiple Dependent							

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description
103	18	203	9	Claims in excess of 20
102	84	202	42	Independent claims in excess of 3
104	280	204	140	Multiple dependent claims, if not paid
109	84	209	42	** Reissue independent claims over original patent
110	18	210	9	** Reissue claims in excess of 20 and over original patent

SUBTOTAL(2) ($) 0.00

**or number previously paid, if greater, For Reissues, see above*

FEE CALCULATION (continued)

3. ADDITIONAL FEES

Large Entity Fee Code	Large Entity Fee ($)	Small Entity Fee Code	Small Entity Fee ($)	Fee Description	Fee Paid
105	130	205	65	Surcharge – late filing fee or oath	
127	50	227	25	Surcharge – late provisional filing fee or cover sheet	
139	130	139	130	Non-English specification	
147	2,250	147	2,250	For filing a request for *ex parte* reexamination	
112	920*	112	920*	Requesting publication of SIR prior to Examiner action	
113	1,840*	113	1,840*	Requesting publication of SIR after Examiner action	
115	110	215	55	Extension for reply within first month	
116	400	216	200	Extension for reply within second month	
117	920	217	460	Extension for reply within third month	
118	1,440	218	720	Extension for reply within fourth month	
128	1,960	228	980	Extension for reply within fifth month	
119	320	219	160	Notice of Appeal	
120	320	220	160	Filing a brief in support of an appeal	160.00
121	280	221	140	Request for oral hearing	
138	1,510	138	1,510	Petition to institute a public use proceeding	
140	110	240	55	Petition to revive - unavoidable	
141	1,280	241	640	Petition to revive - unintentional	
142	1,280	242	640	Utility issue fee (or reissue)	
143	460	243	230	Design issue fee	
144	620	244	310	Plant issue fee	
122	130	122	130	Petitions to the Commissioner	
123	50	123	50	Processing fee under 37 CFR 1.17(q)	
126	180	126	180	Submission of Information Disclosure Stmt	
581	40	581	40	Recording each patent assignment per property (times number of properties)	
146	740	246	370	Filing a submission after final rejection (37 CFR § 1.129(a))	
149	740	249	370	For each additional invention to be examined (37 CFR § 1.129(b))	
179	740	279	370	Request for Continued Examination (RCE)	
169	900	169	900	Request for expedited examination of a design application	
Other fee (specify)					

* Reduced by Basic Filing Fee Paid

SUBTOTAL(3) ($) 160.00

SUBMITTED BY

Name *(Print Type)* *(Attorney/Agent)*	*Jennifer L. Skord*	Registration No. 30,687	Telephone	*919-286-8000*
Signature	*Jennifer L. Skord*		Date	*April 21, 2003*

Complete *(if applicable)*

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re application of:	Bass, Ralph L.	Docket Number:	014123-0[illegible]8
Application Number:	**09/721,131**	Art Unit:	1616
Filed:	November 22, 2000	Examiner:	Frank Choi
For:	METHOD FOR TREATING HIV		

#13
4/30/03

Commissioner for Patents
Box Appeal
Washington, DC 20231

APPEAL BRIEF UNDER 37 CFR 1.192

Sir:

This is an Appeal from the Final Rejection dated August 23, 2002, as reiterated in the Examiner's Advisory, dated March 21, 2003. A Notice of Appeal was filed February 21, 2003. Thus, the due date for filing the Appeal Brief is up to and including **April 21, 2003**.

This Appeal Brief and its attachment of the Appendix (of the claims on appeal) are enclosed here in triplicate. Also, Abstracts of 38 journal articles are enclosed in triplicate.

Additionally enclosed is a check for $160.00 for the small entity fee for the Appeal Brief.

Favorable reconsideration is respectfully requested in view of the following.

REAL PARTY IN INTEREST

The real party in interest is the appellant and inventor, Ralph L. Bass, as the subject application serial no. 09/721,131 has not been assigned.

RELATED APPLICATIONS

There are no other appeals nor interferences known to appellant or appellant's legal representative which will directly affect or be directly affected by or have a bearing on the Board's decision in the instant pending Appeal.

STATUS OF CLAIMS

By Amendment A, dated May 13, 2003, originally filed claims 1 – 22 were canceled and replaced with new claims 22 – 42, the latter being the presently pending claims on Appeal.

Claims 22 – 42 stand finally rejected under 35 U.S.C. §101 for lack of credible utility.

Claim 35 stands finally rejected under 35 U.S.C. §112, first paragraph, for lack of enablement vis-a-vis transdermal administration.

STATUS OF AMENDMENTS AFTER FINAL REJECTION

No amendments were filed subsequent to Final Rejection.

SUMMARY OF INVENTION

The present invention, as defined in claim 22 (the only independent claim), is directed to administering a sodium chloride formulation to an HIV-infected person, where the amount of sodium chloride is more than the person's average daily intake but less than the toxic amount (defined as measured by TCLo and as measured by LD50), and periodically repeating the administration, thereby achieving alleviation of the HIV infection.

Support is at lines 3 – 23 of page 11 and line 19 of page 12 through line 2 of page 13 of appellant's specification.

The present invention, as defined in dependent claim 28 (wherein claim 28 depends back to dependent claim 27, which is directed the sodium chloride formulation being in a mixture with a form of potassium and which depends back to independent claim 22), is directed to the mixture of sodium chloride and potassium containing another ingredient selected from sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, selenium, or combinations thereof.

Support is at lines 6 – 14 of page 9 of appellant's specification.

The present invention, as defined in dependent claim 35, is directed to various types of administration of a solid formulation of the sodium chloride, namely oral, sublingual, buccal, transdermal, or a combination thereof.

Support is at lines 6 – 15 of page 5 of appellant's specification.

ISSUES

Issue 1. Is credible utility under 35 U.S.C. §101 lacking for independent claim 22 and claims 23 – 42 dependent back thereto, wherein claim 22 is directed to periodic administration of a sodium chloride formulation to an HIV-infected person in an amount more than the person's average daily intake but less than the toxic amount (defined as measured by TCLo and as measured by LD50) to achieve alleviation of the HIV infection, because the Laboratory Examples, which illustrate this periodic administration to achieve alleviation of the HIV infection, are prophetic?

Issue 2. Is enablement under 35 U.S.C. §112, first paragraph, lacking for transdermal administration as per dependent claim 35, wherein claim 35 is directed to various types administration of a solid formulation of sodium chloride, namely oral, sublingual, buccal, transdermal, or a combination thereof, because there are no Laboratory Examples illustrating transdermal administration, although appellant's specification at lines 13 – 15 of page 5 indicates that a "good discussion of transdermal administration can be seen in U.S. Patent No. 5,016,652"?

Issue 3. Is credible utility under 35 U.S.C. §101 lacking for dependent claim 28 (which depends back dependent claim 27 which depends back to independent claim 28), wherein dependent claim 27 is directed the sodium chloride formulation being in a mixture with a form of potassium and claim 28 is directed to the mixture of sodium chloride and potassium containing another ingredient selected from sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, selenium, or combinations thereof, when recent research studies (mostly in vivo studies of HIV infected persons and a few in vitro studies) as published in various journals, report a correlation between the presence of nutrient deficiency for each of the nutrients recited in claim 28 and a decrease in the ability to inhibit HIV?

GROUPING OF CLAIMS

Claim 28 does not stand or fall together with the remaining claims 22 - 27 and 29 - 42.

ARGUMENT

Discussion of rejection of claims 22 - 42 under 35 U.S.C. §101 for lack of credible utility.

That sodium chloride, potassium, sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and selenium, each of which is recited in one or more of appellant's claims, *are all nutrients required by the human body*, is to be kept in mind during the following discussion.

In the Final Rejection, the Examiner stated that the claimed alleviation of HIV infection in a human infected with HIV by administration of sodium chloride appears to have specific and substantial utility.

However, the Examiner noted in the Final Rejection that the specification does not appear to show any working examples, but appears to provide only hypothetical statements of what would occur.

Additionally, the Examiner commented in the Final Rejection that it was not shown by what mechanism, theoretical or otherwise, that administration of sodium chloride results in reduction of HIV infection.

Also, the Examiner stated in the Advisory that appellant "does not appear to provide sufficient evidence as to why one of ordinary skill in the art would conclude from the Merck manual [*sic*, brochure] that an HIV [cell] attached to a CD4 T-cell [in the human body] would act differently from free HIV [cells] in phosphate buffered saline."

Appellant respectfully reiterates that the Examiner is ignoring two important legal premises of the U.S. Patent Laws:

1. There is no legal requirement for actual working examples; therefore, prophetic examples are acceptable. The reason is that the filing of an application constitutes a constructive reduction to practice of the invention. See, *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co.*, 224 U.S.P.Q. 409 (Fed. Cir. 1984).

2. There is no legal requirement for an inventor to set forth correctly, or even to know, how or why the invention works. See, *In Re Cortright*, 49 U.S.P.Q.2d 1464, 165 F.3d 1353 (Fed. Cir. 1999).

In connection with prophetic examples instead of working examples, Appellant respectfully reiterates the following vis-à-vis the distinction between an enablement issue under 35 U.S.C. §112, first paragraph, and a credible utility issue under 35 U.S.C. §101. See, both *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., supra,* and *In Re Cortright, supra.*

In connection with enablement under 35 U.S.C. §112, first paragraph, appellant respectfully reiterates that his prophetic Laboratory Examples and specification teach in great detail periodic administration of a certain amount of sodium chloride (more than the person's average daily intake, but less than the toxic amount which would kill the person, i.e., less than the amount of sodium chloride as measured by TCLo and as measured by LD50) to an HIV-infected person in order to alleviate the HIV infection.

Thus, the specification and prophetic examples are clearly sufficient to teach the person of ordinary skill in the art how to make and to use appellant's invention, without undue experimentation. And that is why the Examiner *dropped* the rejection of all of the claims that the Examiner had made in the first Official Action for lack of enablement under 35 U.S.C. §112, first paragraph.

As previously stated, *although appellant does not intend to be bound to any theory, appellant believes the following describes the how and the why, i.e., the mechanism, of his invention.*

As is well known to those of ordinary skill in the art of medicine, immunology, and the like, HIV virus cells have a relatively small size and human cells have a relatively large size.

To assist the Examiner in understanding this size difference, appellant forwarded the Merck brochure entitled "Livin'It" describing their drug CRIXIVAN® for treatment of HIV infection. The first two pages of the Merck brochure have a drawing that shows the smaller HIV virus cell in red attached to the larger human CD4 T-cell in blue. The Merck brochure also discusses how an HIV infection occurs. The HIV virus cell cannot replicate on its own because

does not have DNA but rather has only viral RNA. Thus, the small HIV virus cell attaches itself to the large human CD4 T-cell, replicating by using the DNA of the human CD4 T-cell.

Appellant *theorizes* that how and why his invention works is that the administration of sodium chloride beyond the average daily intake, but less than the toxic amount, should not disrupt the larger human cells, but should be enough to disrupt the smaller HIV virus cells. In other words, this particular amount of sodium chloride should result in a change in osmotic pressure that dehydrates the smaller HIV cells. They should thus be ruptured. Since the particular amount of sodium chloride is still less than the toxic amount, the particular amount should not be enough for rupturing the larger human body cells by a change in osmotic pressure resulting in dehydration.

Accordingly, the disruption/rupturing of the smaller HIV cells should cause them to be removed from the larger human cells, thereby alleviating the HIV infection.

Vis-a-vis the rejection under 35 U.S.C. §101, the Examiner stated in the Final Rejection that:

> Applicant indicates that the administration should result in circulating levels of NaCl within the range of about 0.05 μM to about 1.0 μM and that the extra amount of NaCl will disrupt the HIV virus. [However,] In Hrinda et al. (US Pat. 5,661,023) it is disclosed that NaCl concentrations as high as 1.4 M for prolonged periods, such as greater than 18 hours, only resulted in partial disassembling of HIV particles with dilution to 0.25 M being sufficient to prevent the same (Hrinda et al., Column 8, lines 51 - 68, Column 9, lines 1 - 12). Thus, it appears that the effective amount of NaCl need to disrupt the HIV virus far exceeds what is disclosed and claimed as being the effective therapeutic range as well as the level of NaCl which would be considered to be safe in humans.

Appellant respectfully reiterates that the Examiner has misconstrued how the Hrinda et al. elution process for obtaining HIV particles relates to the present invention.

More specifically, Hrinda et al. inactivate HIV particles by beta-propriolactone (BPL) for about 18 – 24 hours, followed by flowing the BPL-treated HIV particles through a membrane to concentrate them. The concentrated HIV particles are then buffered with phosphate buffered saline (PBS), i.e., an aqueous solution of sodium chloride buffered with phosphate.

The PBS containing the HIV particles is then passed through columns filled with an anion exchange resin, such as TMAE FRACTOGEL®. The HIV particles attach to the TMAE

FRACTOGEL® resin and are subsequently washed with an aqueous solution containing 0.1 - 0.55 M sodium chloride, buffered at a pH of 6 - 7.5.

The attached HIV particles are eluted off the resin using a higher sodium chloride concentration at 0.6 - 2 M, preferably 0.8 - 1.4 M, at the same buffered pH of 6 - 7.5. The eluted solution containing the retroviral particles, particularly HIV, is diluted to reduce the sodium chloride concentration to within the range of 0.05 - 0.25 M. Hrinda et al. state that this is to prevent the partial disassembling of the HIV-1 particles when exposed to the eluant's high sodium chloride concentration for prolonged periods of time, such as greater than 18 hours.

In other words, the sodium chloride concentrations noted by the Examiner, namely "concentrations as high as 1.4 M for prolonged periods, such as greater than 18 hours" that Hrinda et al. use in order avoid partially disassembling HIV particles, are concentrations for HIV particles floating in phosphate buffered aqueous sodium chloride.

In contrast, appellant's desirable circulating levels of sodium chloride within a range of about 0.05 μM to about 1.0 μM, as set out at lines 11 and 12 of page 12 of appellant's specification, are concentrations in human blood in a human body for HIV particles attached to human CD4 T-cells, not for HIV particles floating in phosphate buffered aqueous sodium chloride.

The Examiner has now stated in the Advisory that appellant:

> does not appear to provide sufficient evidence as to why one of ordinary skill in the art would conclude from the Merck manual [*sic*, brochure] that an HIV [cell] attached to a CD4 T-cell [in the human body] would act differently from free HIV [cells] in phosphate buffered saline.

Appellant respectfully points out that the person of ordinary skill in the art will know that phosphate buffered saline solution is not coursing through the veins and arteries of the human body, nor are HIV cells free floating in the human body. Furthermore, that person will be aware of how HIV infects a person (for instance, the explanation in the Merck brochure).

As a result, the person of ordinary skill in the art would expect that HIV cells attached to CD4 T-cells in the human body should act differently from free HIV cells floating in phosphate buffered saline.

Accordingly, based upon current scientific understanding, the person of ordinary skill in the art would expect the claimed invention to function in the disclosed manner, as a treatment for HIV infection in a human, as is clearly illustrated by the prophetic examples and the specification. That person would not expect HIV particles attached to human CD4 T-cells to behave like the Hrinda et al. disclosure of HIV particles free floating in phosphate buffered aqueous sodium chloride.

However, it is also respectfully pointed out that Hrinda et al. did show the phosphate buffered saline removed the HIV cells from the TMAE FRACTOGEL® resin, and appellant does theorize that the particular amount of sodium chloride formulation will remove the HIV cells from the human CD4 T-cells. Thus, one could also argue in the alternative that the Hrinda et al. disclosure of HIV cells removed from TMAE FRACTOGEL® resin by phosphate buffered aqueous sodium chloride is supportive of appellant's theory of how and why his invention works.

In other words, one could argue that, based upon current scientific understanding, the person of ordinary skill in the art would expect the claimed invention to function in the disclosed manner, as a treatment for HIV infection in a human as is clearly illustrated by the prophetic examples and the specification because that person would be aware of how HIV infects a person (for instance, the explanation in the Merck brochure) and as a result, that person would expect HIV particles attached to human CD4 T-cells to behave like and be removed like the Hrinda et al. disclosure of HIV particles removed by a phosphate sodium chloride solution from TMAE FRACTOGEL® resin.

Nevertheless, it does not matter because what appellant stated with respect to the sodium chloride disrupting the HIV cells is only a theory of how the invention works. Appellant has no claims requiring that this mechanism is in fact how his invention works.

There is no legal requirement for an inventor to set forth correctly, or even to know, how or why the invention works. See, *In Re Cortright, supra.*

In summary vis-à-vis credible utility under 35 U.S.C. §101 and enablement under 35 U.S.C. §112, first paragraph, appellant respectfully reiterates the following with respect to *In Re Cortright, supra.*

Cortright's patent application, which eventually matured into her U.S. Patent No. 6,033,676, involved rubbing 8-hydroxy-quinoline sulfate, the active agent in Bag Balm®, into the scalp to treat baldness.

Cortright's claim 15 set out as claim requirements her **surmised theory** of how to use her invention. More particularly, claim 15 required offsetting the effects of lower levels of a male hormone being supplied by arteries to the papilla of scalp hair follicles with the active agent 8-hydroxy-quinoline sulfate, to cause hair to grow again on the scalp, by rubbing into the scalp the ointment having the active agent 8-hydroxy-quinoline sulfate 0.3 % carried in a petrolatum and lanolin base so that the active agent reaches the papilla.

The Court of Appeals specifically stated that it is not a requirement of patentability that an inventor correctly set forth, or even know, how or why the invention works. Thus, Cortright was not required to prove the cause of the hair growth, and claim 15 was not invalid for lack of utility under 35 U.S.C. §101.

However, Cortright's application had no laboratory data, either prophetic or actual, showing that the effects of lower male hormone levels had been offset by Bag Balm® nor even if Bag Balm® had reached the papilla, as required by the language in claim 15. Moreover, the "GENERAL" section at the end of her specification (see, line 50 of column 2 of U.S. Patent No. 6,033,676 to Cortright) started with "Applicant surmises..." prefacing the discussion of offsetting lower male hormone levels by reaching the papilla. Hence, her specification clearly set out that this mechanism was only a theory, not a teaching of how to use. Thus, claim 15 was invalid for not satisfying the how to use requirement of 35 U.S.C. §112, first paragraph.

In contrast, the present appellant's claims do **not** set out as claim requirements appellant's **surmised theory** of how to use his invention by the sodium chloride disrupting the relatively smaller HIV cell, and removing it from the relatively larger human cell.

Thus, there is no need for working examples, nor anything else, for appellant to prove how his invention works.

The Examiner noted in the Advisory that Cortright had working examples.

Appellant respectfully points out that Cortright's working examples were for her other claim which issued in her U.S. Patent No. 6,033,676, not for rejected claim 15.

The Examiner further noted in the Advisory that Cortright lost on 35 U.S.C. §112, first paragraph.

Appellant respectfully points out that other than the rejection of appellant's claim 35 with regard to alleged lack of enablement for transdermal administration, there are no outstanding rejections of appellant's claims under 35 U.S.C. §112, first paragraph. The Examiner withdrew those rejections after the Response to the first Official Action and did not maintain them in the Final Rejection.

The Examiner also stated in the Advisory that a method of alleviating HIV infection by administration of sodium chloride is inherently suspect.

Appellant respectfully points out that treating HIV infection was once considered an inherently unbelievable undertaking, but since then, treatments for HIV infection have gained acceptance, and both AZT (zidovudine) and 3TC (lamivudine) are recognized as effective for treating HIV infection. Similarly, the Court of Appeals in *In Re Cortright, supra* noted that treating baldness was once considered an inherently unbelievable undertaking, but since then, treatments for baldness have gained acceptance, and ROGAINE® (minoxidil) and PROPECIA® (finasteride) are recognized as effective for treating baldness.

Regardless, appellant respectfully submits that it is unlikely that the person of ordinary skill in the art would base a conclusion of existence of credible utility or lack of credible utility on whether HIV cells in the body behave like HIV cells in phosphate buffered saline.

Appellant has recently conducted further research and found 38 recent research studies (mostly in vivo studies for HIV-infected persons and a few in vitro studies) as published in various journals (copies of Abstracts of 38 such publications enclosed). These 38 research studies have reported a correlation between a decrease in the ability of HIV-infected persons to inhibit HIV and the presence in these HIV-infected persons of a deficiency for various nutrients, such as sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and selenium. (The research studies do not address the nutrients, sodium chloride and potassium.)

Appellant respectfully submits that the person of ordinary skill in the art would know that sodium chloride is a nutrient and so are potassium, sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and selenium. Also, the person of ordinary skill in the art would be aware of many, if not all, of these 38 research studies. Thus, on the basis of those research studies, the person of ordinary skill in the art would conclude credible utility exists for appellant's invention.

Accordingly, appellant respectfully requests the Board to instruct the Examiner to withdraw the rejection of claims 22 - 42 under §101.

Discussion of separate patentability for dependent claim 28, which is included in the Examiner's rejection of claims 22 - 42 under 35 U.S.C. §101 for lack of credible utility.

The above arguments vis-à-vis both *Atlas Powder Co. v. E.I. Du Pont De Nemours & Co., supra,* and *In Re Cortright, supra,* are incorporated here by reference, and appellant further points out the following vis-à-vis dependent claim 28.

As noted above, the Examiner stated in the Advisory that appellant:

> does not appear to provide sufficient evidence as to why one of ordinary skill in the art would conclude from the Merck manual [*sic*, brochure] that an HIV [cell] attached to a CD4 T-cell [in the human body] would act differently from free HIV [cells] in phosphate buffered saline.

Would one of ordinary skill in the art base a conclusion of credible utility on whether HIV cells in the body behave like HIV cells in PBS?

No.

One of ordinary skill in the art would also be aware of recent research studies (mostly in vivo studies for HIV-infected persons and a few in vitro studies) as published in various journals (copies of Abstracts of 38 such publications enclosed) that report a correlation between a decrease in the ability to inhibit HIV and the presence in HIV-infected persons of nutrient deficiency for each of the nutrients (sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and selenium) that appellant has recited in his dependent claim 28.

For instance, Kupka et al., "Selenium Status and Mortality among HIV-1-Infected Pregnant Women in Tanzania", Vol. 16, No. 4, *FASEB Journal*, p. A606 (March 20, 2002) shows low plasma selenium levels were associated with increased mortality in HIV-infected persons; Droege et al., "Improvement of Immune Functions in HIV Infection by Sulfur Supplementation: Two Randomized Trials", Vol. 78, No. 1, *Journal of Molecular Medicine*, pp. 55 - 62 (2000) shows administration of sulfur to HIV-infected persons alleviated the HIV infection; Shor-Posner, "Selenium Therapy to Slow HIV Disease Progression in Idus",

Noncompeting Continuation Award (Type 5) supported by National Institute on Drug Abuse, *University of Miami* (2001) shows administration of selenium to HIV-infected persons alleviated the HIV infection; and Eley et al., "Growth and Micronutrient Disturbances in Stable, HIV-Infected Children in Cape Town", Vol. 22, No. 1, *Annals of Tropical Paediatrics*, pp. 19 - 23 (March 2002) shows many HIV-infected children had zinc and copper deficiencies. The Examiner and the Board are invited to browse through all of the 38 enclosed Abstracts.

Thus, one of ordinary skill in the art would conclude that appellant's invention as per dependent claim 28 for having the mixture of sodium chloride and potassium that is periodically administered to an HIV-infected person contain one of more of these nutrients (sulfur, phosphorus, zinc, manganese, iron, copper, chromium, iodine, magnesium, cobalt, and/or selenium) would be credible for treatment of HIV, and hence that person would conclude that credible utility is most certainly present for dependent claim 28.

Accordingly, appellant respectfully requests the Board to instruct the Examiner to withdraw the rejection of claims 27 - 28 under §101.

Discussion of rejection of claim 35 under §112, first paragraph, for the specification not enabling transdermal administration.

The Examiner stated in the Final Rejection that his reason for the rejection of claim 35 was that the specification does not provide enablement for transdermal administration. As support, the Examiner cited the journal article entitled "Salt Water Soaking Possible Alternative Psoriasis Treatment" from *Dermatology Times*, which contains a statement that there was no transdermal uptake of sodium chloride from a *salt bath.*

Appellant respectfully reiterates that the Examiner appears not to understand transdermal administration although the Examiner is correct with respect to what the journal article states.

Soaking in a salt bath only provides for *topical administration* of sodium chloride. Thus, no transdermal uptake of sodium chloride from a salt bath is what is expected.

The Examiner has now stated in the Advisory that his reason for the rejection of claim 35 was because there are no Laboratory Examples illustrating transdermal administration.

As explained exhaustively above, there is no requirement for Laboratory Examples. It is only required that the specification teach the person of ordinary skill in the art how to make and how to use the invention, without undue experimentation.

Appellant respectfully reiterates that, as well known to the person of ordinary skill in the art, transdermal administration is effected with a skin patch containing various chemicals, in addition to the agent that it is desired to administer transdermally. Skin patches for transdermal administration of various agents are well known, and appellant is not claiming to have invented transdermal skin patches.

Rather, appellant clearly provided enablement by the reference on lines 13 - 15 of page 5 of his specification vis-a-vis an explanation of transdermal administration being in U.S. Patent No. 5,016,652. Thus, how to make and how to use skin patches for transdermal administration can be readily ascertained from appellant's specification, without undue experimentation.

Therefore, appellant respectfully requests the Board to instruct the Examiner to withdraw the rejection of claim 35 under the first paragraph of §112.

CONCLUSIONS

Appellant respectfully submits that the present invention as claimed is enabled by the specification in such a way as to convey to the person of ordinary skill in the art that applicant had possession of the claimed invention and in such a way as to teach a person of ordinary skill in the art how to make and/or how to use the invention without undue experimentation. The filing of the application with prophetic Laboratory Examples is a constructive reduction to practice. Accordingly, appellant respectfully requests the Board to instruct the Examiner to withdraw his comments vis-à-vis the lack of working examples.

Moreover, appellant respectfully submits that the present invention as claimed has credible utility, as there is no requirement that an inventor set forth, or know how or why the invention works. Thus, appellant respectfully requests the Board to instruct the Examiner to withdraw the rejection of claims 22 - 44 under §101.

Also, appellant respectfully submits that transdermal administration is clearly enabled. Hence, appellant respectfully requests the Board to instruct the Examiner to withdraw the rejection of claim 35 under the first paragraph of §112.

Appellant respectfully submits that the present application is in proper condition for allowance and respectfully requests the Board to instruct the Examiner to issue official notification of allowance.

DEPOSIT ACCOUNT

Although a check in the amount of $160.00 is enclosed for the fee for the Appeal Brief and it is believed that no further fee is due, the Commissioner is hereby authorized to charge any deficiencies of payment associated with this Communication, or to credit any overpayment, to Deposit Account No. 13-4365.

Respectfully submitted,

Moore & Van Allen PLLC

Date: April 21, 2003

By: Jennifer L. Skord

Jennifer L. Skord
Registration Number: 30,687
Suite 800
2200 West Main Street
Durham, NC 27705
Telephone: 919-286-8000

JLS/js

Enclosures:
Check in the amount of $160 (small entity) for fee for Appeal Brief
In triplicate, Appeal Brief and its Appendix (of claims pending on Appeal)
In triplicate, copies of Abstracts for the following 38 journal articles:

1. Rubio et al., "Reference Values of Selenium in Plasma in Population from Barcelona. Comparison with Several Pathologies", Vol. 16, No. 2, *Journal of Trace Elements in Medicine and Biology*, pp. 231 - 237 (2002).
2. Kupka et al., "Selenium Status and Mortality among HIV-1-Infected Pregnant Women in Tanzania", Vol. 16, No. 4, *FASEB Journal*, p. A606 (March 20, 2002).
3. Eley et al., "Growth and Micronutrient Disturbances in Stable, HIV-Infected Children in Cape Town", Vol. 22, No. 1, *Annals of Tropical Paediatrics*, pp. 19 - 23 (March 2002).
4. Lai et al., "Plasma Zinc, Copper, Copper:Zinc Ratio, and Survival in a Cohort of HIV-1-Infected Homosexual Men", Vol. 27, No. 1, *Journal of Acquired Immune Deficiency Syndromes*, pp. 56 - 62 (May 1, 2001).

5. Baeten et al., "Selenium Deficiency is Associated with Shedding of HIV-1-Infected Cells in the Female Genital Tract", Vol. 26, No. 4, *Journal of Acquired Immune Deficiency Syndromes*, pp. 360 - 364 (April 1, 2001).
6. Marquis et al., "Reported Micronutrient Intakes among HIV-Positive and HIV-Negative Adolescents and Young Adults in the REACH Study", Vol. 15, No. 4, *FASEB Journal*, p. A624 (March 7, 2001).
7. Droege et al., "Improvement of Immune Functions in HIV Infection by Sulfur Supplementation: Two Randomized Trials", Vol. 78, No. 1, *Journal of Molecular Medicine*, pp. 55 - 62 (2000).
8. Zhang et al., "Neuropsychological Performance in Relationship to Selenium Status in the Miami HIV-1 Infected Drug Abusers (MIDAS) Study", Vol. 25, No. 1 - 2, *Society for Neuroscience Abstracts*, p. 43 (1999).
9. Sabbioni et al., "Effects of Trace Metal Compounds on HIV-1 Reverse Transcriptase: An In Vitro Study", Vol. 68, No. 2, *Biological Trace Element Research*, pp. 107 - 120 (May 1999).
10. Fawzi, "Trials of Vitamins in HIV Progression and Transmission", Noncompeting Continuation Award (Type 5) supported by National Institute of Child Health and Human Development, *Harvard University School of Public Health* (2001).
11. Baum, "Zinc Therapy in Zinc Deficient HIV+ Drug Users", New Award (Type 1) supported by National Institute on Drug Abuse, *Florida International University School of Health* (2001).
12. Shor-Posner, "Neuroprotection with Selenium Therapy in HIV+ Idus", Noncompeting Continuation Award (Type 5) supported by National Institute on Drug Abuse, *University of Miami* (2001).
13. Shor-Posner, "Selenium Therapy to Slow HIV Disease Progression in Idus", Noncompeting Continuation Award (Type 5) supported by National Institute on Drug Abuse, *University of Miami* (2001).
14. Izquierdo et al., "Diet Survey and Evaluation of Ingested Nutrients in a Group of HIV Patients", Vol. 17, *Nutrition Hospital*, pp. 97 - 106 (March - April 2002).
15. Woods et al., "Nutrient Intake and Body Weight in a Large HIV Cohort that Includes Women and Minorities", Vol. 102, *Journal of American Diet Association*, pp. 203 - 211 (February 2002).
16. Villamor et al., " Vitamin A Supplements Ameliorate the Adverse Effect of HIV-1, Malaria, and Diarrheal Infection on Child Growth", Vol. 109, *Pediatrics*, p. E6 (January 2002).
17. Duggan et al., "Micronutrients and Child Health: Studies in International Nutrition and HIV Infection", Vol. 59, No. 11, *Nutrition Review*, pp. 358 - 369 (November 2001).
18. Hicar et al., "Structure of the Human Zinc Finger Protein HIVEP3: Molecular Cloning, Expression, Exonintron Structure, and Comparison with Paralogous Genes HIVEP1 and HIVEP2", Vol. 71, *Genomics*, pp. 89 - 100 (January 1, 2001).
19. Bogden et al., "Status of Selected Nutrients and Progression of Human Immunodeficiency Virus Type 1 Infection", Vol. 72, No. 3, *American Journal of Clinical Nutrition*, No. 809 - 815 (September 2002).

20. Breitkreutz et al., "Improvement of Immune Functions in HIV Infection by Sulfur Supplementation: Two Randomized Trials Ysee Comments", Vol. 78, No. 1, *Journal of Molecular Medicine*, pp. 55 – 62 (2000).
21. "A Recent Study Shows Selenium Supplementation Benefits HIV Patients: Selenomax Decreases Risk of Development of Depressed-Dejected Mood State Ynews", Vol. 11, No. 2, *Journal of the Association of Nurses AIDS Care*, p. 103 (March – April 2000).
22. Heller et al., "Development of an Instrument to Assess Nutritional Risk Factors for Children Infected with Human Immunodeficiency Virus", Vol. 100, No. 3, *Journal of the American Diet Association*, pp. 323 - 329 (March 2000).
23. Mocchegiani et al., "Contribution of Zinc to Reduce CD4+ Risk Factor for 'Severe' Infection Relapse in Aging: Parallelism with HIV", Vol.21, No. 4, *International Journal of Immunopharmacology*, pp. 271 - 281 (April 1999).
24. Kuehn et al., "Hypocalcaemia in HIV Infection and AIDS", Vol. 245, No. 1, *Journal of Internal Medicine*, pp. 69 - 73 (January 1999).
25. Look et al., "Sodium Selenite and N-Acetylcysteine in Antiretroviral-Naive HIV-1 Infected Patients: A Randomized, Controlled Pilot Study", Vol. 28, No. 5, *European Journal of Clinical Investigation*, pp. 389 - 397 (May 1998).
26. Allard et al., "Oxidative Stress and Plasma Antioxidant Micronutrients in Humans with HIV Infection Ysee Comments", Vol. 67, No. 1, *American Journal of Clinical Nutrition*, pp. 143 - 147 (January 1998).
27. Henderson et al., "Serum and Plasma Markers of Nutritional Status in Children Infected with the Human Immunodeficiency Virus", Vol. 97, No. 12, *Journal of the American Diet Association*, pp. 1377 - 1381 (December 1997).
28. Ioannidis et al., "The Impact of High-Risk Patients on the Results of Clinical Trials", Vol. 50, No. 10, *Journal of Clinical Epidemiology*, pp. 1089 - 1098 (October 1997).
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30. Chariot et al., "Muscle Involvement in Human Immunodeficiency Virus-Infected Patients in Associated with Marked Selenium Deficiency", Vol. 20, No. 3, *Muscle Nerve*, pp. 386 - 389 (March 1997).
31. Constans et al., "One-Year Antioxidant Supplementation with Beta-Carotene or Selenium for Patients Infected with Human Immunodeficiency Virus: A Pilot Study", Vol. 23, No. 3, *Clinical Infectious Disease*, pp. 654 - 656 (September 1996).
32. Tang et al., "Effects of Micronutrient Intake on Survival in Human Immunodeficiency Virus Type 1 Infection", Vol. 143, No. 12, *American Journal of Epidemiology*, pp. 1244 - 1256 (June 15, 1996).
33. Rivard et al., "Synoviorthesis with Colloidal 32P Chromic Phosphate for the Treatment of Hemophilic Arthropathy Ysee Comments", Vol. 76, No. 4, *Journal of Bone Joint Surgery Am*, pp. 482 - 488 (April 1994).
34. Tang et al, "Dietary Micronutrient Intake and Risk of Progression to Acquired Immunodeficiency Syndrome (AIDS) in Human Immunodeficiency Virus Type 1 (HIV-1)-Infected Homosexual Men", Vol. 138, No. 11, *American Journal of Epidemiology*, pp. 937 - 951 (December 1, 1993).

35. York et al., "Molecular Modeling Studies suggest that Zinc Ions Inhibit HIV-1 Protease by Binding at Catalytic Aspartates", Vol. 101, No. 3, *Environmental Health Perspective*, pp. 246 - 250 (August 1993).
36. Moore et al., "Role of Nutritional Status and Weight Loss in HIV Seroconversion among Rwandan Women", Vol. 6, No. 6, *Journal of Acquired Immune Deficiency Syndrome*, pp. 611 - 616 (June 1993).
37. McCorkindale et al., "Nutritional Status of HIV-Infected Patients during the Early Disease Stages", Vol. 90, No. 9, *Journal of American Diet Association*, pp. 1236 - 1241 (September 1990).
38. Graham et al., "Relationship of Serum Copper and Zinc Levels to HIV-1 Seropositivity and Progression to AIDS", Vol. 4, No. 10, *Journal of Acquired Immune Deficiency Syndrome*, pp. 976-980 (1991).

In re application of:	Bass, Ralph L.	Docket Number:	014123-000008
Application Number:	09/721,131	Art Unit:	1616
Filed:	November 22, 2000	Examiner:	Frank Choi
For:	Method for Treating HIV		

CERTIFICATE OF MAILING/TRANSMISSION (37 C.F.R. § 1.8(a))

I hereby certify that this correspondence is, on the date shown below, being:

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Signature: Lillian S. Glenn

Lillian S. Glenn
(Name of person certifying)

Date: April 21, 2003

APPENDIX
(Claims on Appeal for Application Serial No. 09/721,131)

22. A method for providing sodium chloride to a human having HIV infection by administering to the upper gastro-intestinal tract of the human a selected amount of a formulation of sodium chloride, said method comprising:

(a) administering the sodium chloride formulation to the human's upper gastro-intestinal tract so as to introduce the sodium chloride formulation to the metabolism of the human, wherein the amount of the sodium chloride in the sodium chloride formulation administered is (i) sufficient to provide more sodium chloride than the human's average daily intake for sodium chloride, as determined after monitoring the human for about 1 month, (ii) less than a toxic amount measured by TCLo, the dosage for oral consumption that is the lowest dosage of sodium chloride that has produced toxic side effects in humans, and (iii) less than a toxic amount measured by LD50, the dosage of sodium chloride that is lethal for 50% of the human population;

(b) periodically repeating (a), so as to administer a therapeutically effective amount of the sodium chloride formulation to the human's metabolism; and

(c) achieving alleviation of the HIV infection.

23. The method of claim 22, wherein the sodium chloride formulation is free of having other medicaments incorporated therewith for treatment of HIV infection.

24. The method of claim 22, wherein steps (a) and (b) are accomplished at least once per day.

25. The method of claim 22, wherein the amount of the sodium chloride formulation administered is sufficient to provide at least about 250 mg per day more sodium chloride than the human's average daily intake for sodium chloride, as determined after monitoring the human for about 1 month.

26. The method of claim 25, wherein the amount of the sodium chloride formulation administered and the average daily intake for sodium chloride provide at least 7500 mg/day of sodium chloride.

27. The method of claim 22, wherein the sodium chloride formulation is a mixture with a form of potassium in a weight ratio amount of Na:K up to about 1:1.

28. The method of claim 27, wherein the mixture contains up to about 20% by weight of another ingredient selected from the group consisting of S, P, Zn, Mn, Fe, Cu, Cr, I, Mg, Co, Se, and combinations thereof.

29. The method of claim 22, wherein the sodium chloride formulation is free of having other mineral salts incorporated therewith except for trace amounts thereof.

30. The method of claim 22, wherein the sodium chloride formulation is in a form selected from the group consisting of a solid formulation of sodium chloride and a solution formulation of sodium chloride.

31. The method of claim 30, wherein the solid formulation contains from about 55% to about 100% of sodium chloride.

32. The method of claim 31, wherein the solid formulation contains from about 75% to about 100% by weight sodium chloride.

33. The method of claim 30, wherein the solid formulation of sodium chloride is free of having a carrier incorporated therewith.

34. The method of claim 30, wherein the solid formulation of sodium chloride is selected from the group consisting of a tablet, a powder, and a combination thereof.

35. The method of claim 30, wherein administration of the solid formulation of sodium chloride is administration selected from the group consisting of oral, sublingual, buccal, transdermal, and a combination thereof.

36. The method of claim 30, wherein the solution formulation of sodium chloride contains at least about 2% by weight sodium chloride.

37. The method according to claim 30, wherein the solution formulation of sodium chloride is aqueous.

38. The method according to claim 30, further including a flavoring in the solution formulation of sodium chloride to improve palatability.

39. The method according to claim 38, wherein the flavoring is selected from the group consisting of sugar, coffee, beer, wine, whiskey, fruit juice, milk, soda, mint, and combinations thereof.

40. The method of claim 30, wherein administration of the solution formulation of sodium chloride is administration selected from the group consisting of oral, gavage, and a combination thereof.

41. The method according to claim 22, wherein the administration to the upper gastro-intestinal tract is by way of a portion of the upper gastro-intestinal tract selected from the group consisting of a mouth, an esophagus, a stomach, a duodenum, and a combination thereof.

42. The method according to claim 22, further including a minor amount of another ingredient selected from the group consisting of potassium chloride, potassium carbonate, potassium protein complexes, potassium phosphate, sodium carbonate, sodium protein complexes, sodium phosphate, and combinations thereof, wherein the total minor amount of said other ingredients is less than about 45% by weight, based on the weight of the sodium chloride.

Jennifer Skord

Citations from BIOLOGICAL ABSTRACTS: BIO

1. NDN 244-0218-7969-0: **Reference values of selenium in plasma in population from Barcelona. Comparison with several pathologies.**

2. NDN 244-0180-1803-6: **Selenium status and mortality among HIV-1-infected pregnant women in Tanzania.**

3. NDN 244-0173-9099-9: **Growth and micronutrient disturbances in stable, HIV-infected children in Cape Town.**

Citations from Biological Abstracts: BO1

4. NDN 199-0118-2833-2: **Plasma zinc , copper, copper:zinc ratio, and survival in a cohort of HIV-1-infected homosexual men.**

5. NDN 199-0111-0447-0: **Selenium deficiency is associated with shedding of HIV-1-infected cells in the female genital tract.**

6. NDN 199-0111-0384-2: **Reported micronutrient intakes among HIV-positive and HIV-negative adolescents and young adults in the REACH study .**

7. NDN 199-0046-0153-4: **Improvement of immune functions in HIV infection by sulfur supplementation: Two randomized trials .**

8. NDN 199-0035-3930-4: **Neuropsychological performance in relationship to selenium status in the Miami HIV-1 infected drug abusers (MIDAS) study .**

9. NDN 199-0002-5178-4: **Effects of trace metal compounds on HIV-1 reverse transcriptase: An in vitro study .**

Citations from Federal Research in Progress (FRP): FRP

10. NDN 049-0545-9172-9: **TRIALS OF VITAMINS IN HIV PROGRESSION AND TRANSMISSION**

11. NDN 049-0543-9812-7: **Zinc Therapy in Zinc Deficient HIV + Drug Users**

12. NDN 049-0543-9063-3: **NEUROPROTECTION WITH SELENIUM THERAPY IN HIV + IDUS**

13. NDN 049-0543-8620-4: **SELENIUM THERAPY TO SLOW HIV DISEASE PROGRESSION IN IDUS**

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14. NDN 222-0367-0305-9: **Diet survey and evaluation of ingested nutrients in a group of HIV patients**

15. NDN 222-0313-5613-8: **Nutrient intake and body weight in a large HIV cohort that includes women and minorities.**

16. NDN 222-0312-2689-9: **Vitamin A supplements ameliorate the adverse effect of HIV-1, malaria, and diarrheal infections on child growth.**

17. NDN 222-0303-3960-1: **Micronutrients and child health: studies in international nutrition and HIV infection.**

18. NDN 222-0235-3723-1: **Structure of the human zinc finger protein HIVEP3: molecular cloning, expression, exon-intron structure, and comparison with paralogous genes HIVEP1 and HIVEP2.**

Citations from MEDLINE(R) DATABASE (1997 TO 2000): ME1

19. NDN 194-0189-3024-1: **Status of selected nutrients and progression of human immunodeficiency virus type 1 infection.**

20. NDN 194-0175-3123-5: **Improvement of immune functions in HIV infection by sulfur supplementation: two randomized trials Ýsee comments¨**

21. NDN 194-0173-8388-0: **A recent study shows selenium supplementation benefits HIV patients: Selenomax decreases risk of development of depressed-dejected mood state Ýnews¨**

22. NDN 194-0166-6594-3: **Development of an instrument to assess nutritional risk factors for children infected with human immunodeficiency virus.**

23. NDN 194-0140-9182-0: **Contribution of zinc to reduce CD4+ risk factor for 'severe' infection relapse in aging: parallelism with HIV .**

24. NDN 194-0123-8149-1: **Hypocalcaemia in HIV infection and AIDS.**

25. NDN 194-0099-6813-9: **Sodium selenite and N-acetylcysteine in antiretroviral-naive HIV-1-infected patients: a randomized, controlled pilot study .**

26. NDN 194-0073-7686-5: **Oxidative stress and plasma antioxidant micronutrients in humans with HIV infection Ýsee comments¨**

27. NDN 194-0069-3796-0: **Serum and plasma markers of nutritional status in children infected with the human immunodeficiency virus.**

28. NDN 194-0067-2701-0: **The impact of high-risk patients on the results of clinical trials .**

29. NDN 194-0047-1288-0: **Serum selenium versus lymphocyte subsets and markers of disease progression and inflammatory response in human immunodeficiency virus-1 infection.**

30. NDN 194-0035-2060-0: **Muscle involvement in human immunodeficiency virus-infected patients is associated with marked selenium deficiency.**

31. NDN 194-0023-2193-0: **One-year antioxidant supplementation with beta-carotene or selenium for patients infected with human immunodeficiency virus: a pilot study .**

32. NDN 194-0004-7177-7: **Effects of micronutrient intake on survival in human immunodeficiency virus type 1 infection.**

Citations from MEDLINE(R) DATABASE (1993 TO 1997): ME2

33. NDN 193-0040-4870-0: **Synoviorthesis with colloidal 32P chromic phosphate for the treatment of hemophilic arthropathy Ýsee comments¨**

34. NDN 193-0029-8213-2: **Dietary micronutrient intake and risk of progression to acquired immunodeficiency syndrome (AIDS) in human immunodeficiency virus type 1 (HIV-1)-infected homosexual men.**

35. NDN 193-0016-6822-3: **Molecular modeling studies suggest that zinc ions inhibit HIV-1 protease by binding at catalytic aspartates.**

36. NDN 193-0006-9908-0: **Role of nutritional status and weight loss in HIV seroconversion among Rwandan women.**

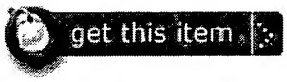
Citations from MEDLINE(R) DATABASE (1990 TO 1993): ME3

37. NDN 192-0099-0708-6: **Nutritional status of HIV-infected patients during the early disease stages.**

38. NDN 192-0042-7146-3: **Relationship of serum copper and zinc levels to HIV-1 seropositivity and progression to AIDS.**

Citations from BIOLOGICAL ABSTRACTS: BIO

1. Reference values of selenium in plasma in population from Barcelona. Comparison with several pathologies.
BIO 06-13 06-138637 NDN- 244-0218-7969-0



Rubio, Roser; Garcia-Beltran, Lydia; Sabe, Rosa

JOURNAL NAME- Journal of Trace Elements in Medicine and Biology
VOL. 16
NO. 4
2002
PP. 231-237.
DOCUMENT TYPE- Article
ISSN- 0946-672X
ADDRESS- E-Mail: roser.rubio@apolo.qui.ub.es, Departament de Quimica Analitica, Universitat de Barcelona, Marti i Franques 1-11, 08028, Barcelona, Spain, Spain
LANGUAGE- ENGLISH

Plasma selenium reference values from healthy donors in the metropolitan area of Barcelona are determined. A random sample from 156 healthy adults (control group) is analysed by using electrothermal atomic absorption spectrometry with Zeeman effect background correction. The relationship between several pathologies and Se content is also evaluated. Se content from 64 samples from subjects with chronic renal failure and 54 from subjects suffering from several malignancies are determined and the results are compared to the reference values. Moreover, Se contents are determined and compared in two groups of children, healthy (19 samples) and children of mothers infected with HIV-1 (16 samples). In the control group, Se plasma concentration ranges between 50 and 145 mugcntdotL-1 (82.2+-17.5 mugcntdotL-1). Significantly Lower values are found in the two pathologies studied (malignancy and chronic renal failure), compared to the control group. However, no significant differences in Se content are found between the two groups studied regarding malignancy and chronic renal failure. In children of mothers infected with HIV-1, Se status is significantly Lower than that of healthy children.

DESCRIPTOR(S)- *Clinical Chemistry (Allied Medical Sciences); *Epidemiology (Population Studies); *Infection; *human (Hominidae) --adult; *human (Hominidae) --Spanish; *HIV-1 Human immunodeficiency virus 1 (Retroviridae) --pathogen; *Animals; *Chordates; *DNA and RNA Reverse Transcribing Viruses; *Humans; *Mammals; *Microorganisms; *Primates; *Vertebrates; *Viruses; *cancer --neoplastic disease; *chronic renal failure --urologic disease; * selenium --plasma reference value; *Zeeman effect background correction --mathematical and computer techniques; *Kidney Failure, Chronic (MeSH); *Neoplasms (MeSH)
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Hominidae --Animalia; Hominidae --Chordata; Hominidae --Mammalia; Hominidae --Primates; Hominidae --Vertebrata; Retroviridae --DNA and RNA Reverse Transcribing Viruses; Retroviridae --Microorganisms; Retroviridae --Viruses
GEOGRAPHIC DESCRIPTOR(S)- Barcelona (Spain, Europe, Palearctic region)
BIOSIS Concept Code(s)- 10006; 10069; 15506; 24004; 33502; 36006; 37052; 37054; 37056

BIOSYSTEMATIC CODES- 03305; 86215
CAS REGISTRY/EC NUMBER(S)- *7782-49-2 --SELENIUM
CHEMICAL INDEXING- print .

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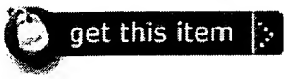
2. Selenium status and mortality among HIV-1-infected pregnant women in Tanzania.
BIO 05-31 05-387263 NDN- 244-0180-1803-6



Kupka, Roland; Fawzi, Wafaie W.; Hunter, David J.; Morris, Steve; Msamanga, Gernard I.; Mugusi, Ferdinand; Spiegelman, Donna

JOURNAL NAME- FASEB Journal
VOL. 16
NO. 4
March 20, 2002
PP. A606.
DOCUMENT TYPE- Meeting
ISSN- 0892-6638
ADDRESS- Department of Nutrition, Harvard School of Public Health, 665 Huntington Avenue, SPH 2, Boston, MA, 02115, USA
CONFERENCE DATE- April 20-24, 2002
CONFERENCE TITLE- Annual Meeting of the Professional Research Scientists on Experimental Biology
LANGUAGE- ENGLISH

In reports from developed countries, low plasma selenium levels were associated increased mortality in HIV-infected individuals but there are no studies from developing countries. We determined plasma selenium concentrations and tracked survival among 950 HIV-positive pregnant women participating in the Tanzania Trial of Vitamins. Mean plasma selenium concentration was 127 mug/l (SD 23). Over the course of the 3.5-year average follow-up, 177 women (19%) died. Mortality rates in the lowest, medium, and highest tertiles of plasma selenium were 13.2%, 18.9%, and 23.7%, respectively (P for trend=0.001). In a Cox proportional hazards model adjusting for baseline body mass index, age, CD4 count and gestational age, women in the lowest tertile had a nearly twofold increased risk of mortality (hazard ratio (HR)=1.94, 95% CI=1.28-2.94), while women in the medium tertile had a 51% increased risk (HR=1.51, 95% CI=0.99-2.33) as compared to women in the highest tertile (P for trend=0.02). These data suggest that selenium may be important for health of HIV-infected individuals. Randomized supplementation trials are needed to determine whether the described association is causal.

DESCRIPTOR(S)- *Epidemiology (Population Studies); *Infection; *Nutrition; *Obstetrics (Human Medicine, Medical Sciences); *human (Hominidae) --female; *human (Hominidae) --host; *human (Hominidae) --patient; *HIV-1 human immunodeficiency virus 1 (Retroviridae) --pathogen; *Animal Viruses; *Animals; *Chordates; *Humans; *Mammals; *Microorganisms; *Primates; *Vertebrates; *Viruses; *HIV-1 infection human immunodeficiency virus 1 infection --immune system disease; *HIV-1 infection human immunodeficiency virus 1 infection --mortality; *HIV-1

infection human immunodeficiency virus 1 infection --viral disease; * selenium --plasma level; *pregnancy; *Meeting Abstract; *HIV Infections (MeSH)
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Hominidae --Animalia; Hominidae --Chordata; Hominidae --Mammalia; Hominidae --Primates; Hominidae --Vertebrata; Retroviridae --Animal Viruses; Retroviridae --Microorganisms; Retroviridae --Viruses
GEOGRAPHIC DESCRIPTOR(S)- Tanzania (Africa, Ethiopian region)
BIOSIS Concept Code(s)- 00520; 10069; 13202; 16506; 33506; 34508; 36006; 37052; 37054; 37056
BIOSYSTEMATIC CODES- 02623; 86215
CAS REGISTRY/EC NUMBER(S)- *7782-49-2 --SELENIUM
CONCEPT CODE(S)- New Orleans, Louisiana, USA
CHEMICAL INDEXING- print .

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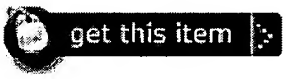
3. Growth and micronutrient disturbances in stable, HIV-infected children in Cape Town.
BIO 05-25 05-324559 NDN- 244-0173-9099-9



Eley, Brian S.; Abelse, Lisa; Cooper, Margaret; Hussey, Gregory D.; Kossew, Glynis; Sive, Alan A.

JOURNAL NAME- Annals of Tropical Paediatrics
VOL. 22
NO. 1
March, 2002
PP. 19-23.
DOCUMENT TYPE- Article
ISSN- 0272-4936
ADDRESS- E-Mail: beley@ich.uct.ac.za, Department of Paediatrics and Child Health, Red Cross Children's Hospital, Rondebosch, 7701, South Africa
LANGUAGE- ENGLISH

This prospective study of 60 stable, HIV-infected children in an economically deprived setting was designed to document anthropometric and micronutrient disturbances. Investigations included CD4+ counts, anthropometry and plasma levels of albumin, transthyretin, retinol-binding protein (RBP), vitamins A, B6, E and B12, and folate, zinc and copper. The median age was 25 months. Thirty-two per cent had mild, 48% moderate and 20% severe clinical features, and 80% were moderately or severely immunosuppressed. Twenty-eight per cent had a weight Z-score < -2.0 and 58% a height Z-score < -2.0. Many children had micronutrient deficiencies: albumin (70%), transthyretin (100%), RBP (85%), vitamins A (80%), B6 (37%), E (37%) and B12 (5%), zinc (20%) and copper (25%). Sixty-two per cent had two or more trace element or vitamin deficiencies. There was a weak association between micronutrient status and disease status. Micronutrient concentrations did not correlate with chronological age, height-for-age or weight-for-age. CRP was elevated in 53% but did not correlate with any of the micronutrient concentrations. Micronutrient deficiencies were more common and micronutrient concentrations lower in children over 24 months of age.

DESCRIPTOR(S)- *Epidemiology (Population Studies); *Infection; *Nutrition; *Pediatrics (Human Medicine, Medical Sciences); *human (Hominidae) --child; *human (Hominidae) --host; *human (Hominidae) --infant; *human (Hominidae) --patient; *HIV human immunodeficiency virus (Retroviridae) --pathogen; *Animal Viruses; *Animals; *Chordates; *Humans; *Mammals; *Microorganisms; *Primates; *Vertebrates; *Viruses; *CD4-positive cells --blood and lymphatics; *CD4-positive cells --count; *CD4-positive cells --immune system; *HIV infection human immunodeficiency virus infection --blood and lymphatic disease; *HIV infection human immunodeficiency virus infection --immune system disease; *HIV infection human immunodeficiency virus infection --viral disease; *albumin; *copper; *folate; *retinol-binding protein; *transthyretin; *vitamin A; *vitamin B-12; *vitamin B-6; *vitamin E; * zinc ; *anthropometry; *growth; *micronutrient disturbance; *HIV Infections (MeSH)
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Hominidae --Animalia; Hominidae --Chordata; Hominidae --Mammalia; Hominidae --Primates; Hominidae --Vertebrata; Retroviridae --Animal Viruses; Retroviridae --Microorganisms; Retroviridae --Viruses
GEOGRAPHIC DESCRIPTOR(S)- Cape Town (South Africa, Africa, Ethiopian region)
BIOSIS Concept Code(s)- 02506; 02508; 10060; 10063; 10064; 10069; 13202; 15002; 15004; 15006; 25000; 33506; 34502; 34508; 36006; 37052; 37054; 37056
BIOSYSTEMATIC CODES- 02623; 86215
CAS REGISTRY/EC NUMBER(S)- *11103-57-4Q --VITAMIN A; *1406-18-4 --VITAMIN E; *68-19-9 --VITAMIN B-12; *68-26-8Q --VITAMIN A; *7440-50-8 --COPPER; *7440-66-6 --ZINC; *8059-24-3 --VITAMIN B-6
CHEMICAL INDEXING- print .

Citations from Biological Abstracts: BO1

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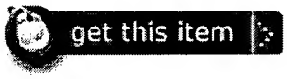
4. Plasma zinc , copper, copper:zinc ratio, and survival in a cohort of HIV-1-infected homosexual men.
BIO 04-32 04-346621 NDN- 199-0118-2833-2



Lai, Hong; Baum, Marianna K.; Lai, Shenghan; Ma, Fangchao; Shor-Posner, Gail; Trapido, Edward

JOURNAL NAME- JAIDS Journal of Acquired Immune Deficiency Syndromes
VOL. 27
NO. 1
May 1, 2001
PP. 56-62.
DOCUMENT TYPE- Article
ADDRESS- Department of Epidemiology, Johns Hopkins University School of Hygiene and Public Health, 615 N. Wolfe Street, Room E6141, Baltimore, MD, 21205: holai@jhsph.edu, USA
LANGUAGE- ENGLISH

A prospective cohort study of 121 HIV-1-positive homosexual men was conducted in Miami,

Florida, U.S.A. to evaluate the associations between plasma zinc and copper levels and mortality. Plasma zinc and copper levels were measured at baseline and then at semiannual visits. Zinc inadequacy and copper inadequacy were defined as plasma zinc levels <75 (mug/dl) and plasma copper levels <85 (mug/dl), respectively. HIV-1-related deaths were confirmed by review of death certificates. Cox proportional hazards regression models with time-dependent covariates were used to estimate the relative risks of zinc and copper inadequacy on mortality. Over the average course of the 3.3-year follow-up, 19 participants (16%) died of HIV-1-related causes. After adjustment for potential confounders, including low CD4+ cell counts and antiretroviral therapy, zinc inadequacy and copper:zinc ratio >1 (i.e., plasma copper level greater than plasma zinc level) were associated with increased mortality (relative risks (RRs); 95% confidence intervals (CIs), 4.98, 1.30-19.00 and 8.28, 1.03-66.58, respectively). A negative association was also observed between plasma zinc levels and mortality (RR 0.94; 95% CI, 0.91-0.98). Plasma levels of copper were not significantly associated with mortality. These results suggest that plasma zinc inadequacy or the plasma copper:zinc ratio may be useful predictors of survival in HIV-1 infection. The latter appears to be a stronger predictor.

DESCRIPTOR(S)- *Clinical Immunology (Human Medicine, Medical Sciences); *Epidemiology (Population Studies); *Infection; *human (Hominidae) --homosexual; *human (Hominidae) --host; *human (Hominidae) --male; *human (Hominidae) --patient; * human immunodeficiency virus-1 HIV-1 (Retroviridae) --pathogen; *Animal Viruses; *Animals; *Chordates; *Humans; *Mammals; *Microorganisms; *Primates; *Vertebrates; *Viruses; *plasma --blood and lymphatics; * human immunodeficiency virus-1 infection --immune system disease; * human immunodeficiency virus-1 infection --viral disease; *copper; * zinc ; *copper --inc ratio; *mortality; *HIV Infections (MeSH)
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Hominidae --Animalia; Hominidae --Chordata; Hominidae --Mammalia; Hominidae --Primates; Hominidae --Vertebrata; Retroviridae --Animal Viruses; Retroviridae --Microorganisms; Retroviridae --Viruses
GEOGRAPHIC DESCRIPTOR(S)- Miami (Florida, USA, North America, Nearctic region)
BIOSIS Concept Code(s)- 10069; 15002; 15004; 33506; 34508; 36006; 37052; 37054; 37056
BIOSYSTEMATIC CODES- 02623; 86215
CAS REGISTRY/EC NUMBER(S)- *7440-50-8 --COPPER; *7440-66-6 --ZINC
CHEMICAL INDEXING- print .

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5. Selenium deficiency is associated with shedding of HIV-1-infected cells in the female genital tract.
BIO 04-25 04-274235 NDN- 199-0111-0447-0

Baeten, Jared M.; Bankson, Daniel D.; Bwayo, Job J.; Hughes, Martin P.; Kreiss, Joan K.; Mandaliya, Kishorchandra; Mostad, Sara B.; Ndinya-Achola, Jeckoniah O.; Overbaugh, Julie

JOURNAL NAME- JAIDS Journal of Acquired Immune Deficiency Syndromes
VOL. 26
NO. 4
April 1, 2001
PP. 360-364.

DOCUMENT TYPE- Article
ADDRESS- University of Washington, 325 Ninth Avenue, Seattle, WA, 98104-2499: jbaeten@u.washington.edu, USA
LANGUAGE- ENGLISH

Objective: To assess the relation between selenium deficiency and vaginal or cervical shedding of HIV-1-infected cells. Design: Cross-sectional study of 318 HIV-1 seropositive women in Mombasa, Kenya. Methods: Vaginal and cervical swab specimens were tested for the presence of HIV-1 DNA by polymerase chain reaction. Multivariate logistic regression models, adjusting for CD4 count and vitamin A deficiency, were used. Results: Selenium deficiency (defined as levels <85 mug/L) was observed in 11% of the study population. In unstratified multivariate analyses, there was no significant association between selenium deficiency and vaginal or cervical shedding. In stratified analyses, however, significant associations became apparent after excluding women with predictors of shedding with strong local effects on the genital tract mucosa. Among women who did not use oral contraceptives and who did not have vaginal candidiasis, selenium deficiency was significantly associated with vaginal shedding (adjusted odds ratio (AOR) 2.9, 95% confidence interval (CI) 1.0-8.8, p = .05). Effect modification was also observed in the relation between selenium deficiency and cervical shedding, with a significant association seen among those women who were not using oral contraceptive pills or depot medroxyprogesterone acetate and who did not have Neisseria gonorrhoeae infection (AOR 2.8, 95% CI 1.1-7.0, p = .02). Conclusions: We found selenium deficiency to be associated with a nearly threefold higher likelihood of genital mucosal shedding of HIV-1-infected cells, suggesting that deficiency may increase the infectiousness of women with HIV-1. Nutritional interventions to prevent HIV-1 transmission warrant investigation.

DESCRIPTOR(S)- *Clinical Immunology (Human Medicine, Medical Sciences); *Epidemiology (Population Studies); *Infection; *Nutrition; *human (Hominidae) --female; *human (Hominidae) --host; *human (Hominidae) --patient; *HIV-1 human immunodeficiency virus 1 (Retroviridae) --pathogen; *Animal Viruses; *Animals; *Chordates; *Humans; *Mammals; *Microorganisms; *Primates; *Vertebrates; *Viruses; *genital tract --reproductive system; *CD4 cell --immune system; * selenium deficiency --nutritional disease; *HIV-1 infection human immunodeficiency virus 1 infection --immune system disease; *HIV-1 infection human immunodeficiency virus 1 infection --viral disease; * selenium ; *viral DNA; *cervical shedding; *vaginal shedding; *HIV Infections (MeSH); *Selenium/deficiency (MeSH)
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Hominidae --Animalia; Hominidae --Chordata; Hominidae --Mammalia; Hominidae --Primates; Hominidae --Vertebrata; Retroviridae --Animal Viruses; Retroviridae --Microorganisms; Retroviridae --Viruses
GEOGRAPHIC DESCRIPTOR(S)- Mombasa (Kenya, Africa, Ethiopian region)
BIOSIS Concept Code(s)- 02506; 02508; 10062; 10069; 13202; 13203; 16504; 31500; 33506; 34502; 34508; 36006; 37052; 37054; 37056
BIOSYSTEMATIC CODES- 02623; 86215
CAS REGISTRY/EC NUMBER(S)- *7782-49-2 --SELENIUM
CHEMICAL INDEXING- print .

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6. Reported micronutrient intakes among HIV-positive and HIV-negative adolescents and young adults in the REACH study .
BIO 04-25 04-274172 NDN- 199-0111-0384-2

Marquis, Grace S.; Kruzich, Laurie A.; Stephensen, Charles B.; Wilson, Craig M.

JOURNAL NAME- FASEB Journal
VOL. 15
NO. 4
March 7, 2001
PP. A624.
DOCUMENT TYPE- Meeting
ISSN- 0892-6638
ADDRESS- Iowa State University, 1127 Human Nutr. Sci. Bldg., Ames, IA, 50011, USA
CONFERENCE DATE- March 31-April 04, 2001
CONFERENCE TITLE- Annual Meeting of the Federation of American Societies for Experimental Biology on Experimental Biology 2001
LANGUAGE- ENGLISH

HIV may increase dietary requirements due to oxidative damage from the chronically active immune system. The increased nutrient needs present a special challenge for HIV-infected adolescents as adolescents generally are known to have poor quality diets. We examined the association between reported micronutrient intake and HIV status, using the Block Food Frequency Questionnaire (98.2 version) with participants of the REACH study, a multi-site cohort study of 301 HIV-infected and 148 HIV-uninfected adolescents. 87% of the REACH sample agreed to be interviewed for this nutrition study; these were 75% female, two-thirds African-American, and 50% overweight or obese. The clinical profile consisted of HIV uninfected and three HIV-infected stages: HIV-infected early, HIV-infected intermediate, and HIV-infected late. The three stages were determined by a combination of CD4+ T cell count, HIV symptoms, and AIDS-defining conditions (CDC criteria). Where appropriate, reported intakes were compared to the U.S. Recommended Dietary Allowances (RDA), using reference values from the 1990 RDA or the 2000 Dietary Reference Intakes. Low reported dietary intakes (<80% RDA) were most common for vitamin E and zinc (41% and 27% of all participants, respectively). Zinc intakes were highest among participants in the intermediate and late HIV infection stages ($p<0.01$). Vitamin E intakes were progressively higher ($p<0.05$) through the intermediate stage of illness; the lowest intakes were in those individuals who were in the late stage of illness. Mean reported micronutrient intake values were above the recommended level of intake; however, there was considerable variation. Inadequate intake of specific antioxidants, such as vitamin E, may be of concern for the HIV+ adolescent and young adult population.

DESCRIPTOR(S)- *Epidemiology (Population Studies); *Infection; *Nutrition; *human (Hominidae) --adolescent; *human (Hominidae) --adult; *human (Hominidae) --host; *HIV human immunodeficiency virus (Retroviridae) --pathogen; *Animal Viruses; *Animals; *Chordates; *Humans; *Mammals; *Microorganisms; *Primates; *Vertebrates; *Viruses; *CD4-positive T cell --blood and lymphatics; *CD4-positive T cell --immune system; *AIDS acquired immunodeficiency syndrome --immune system disease; *AIDS acquired immunodeficiency syndrome --viral disease; *HIV infection human immunodeficiency virus infection --immune system disease; *HIV infection human immunodeficiency virus infection --viral disease; *micronutrient --dietary intake; *vitamin E --dietary intake; * zinc --dietary intake; *Meeting Abstract; *Acquired Immunodeficiency Syndrome (MeSH); *HIV Infections (MeSH)
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Hominidae --Animalia; Hominidae --Chordata; Hominidae --Mammalia; Hominidae --Primates; Hominidae --Vertebrata; Retroviridae --

Animal Viruses; Retroviridae --Microorganisms; Retroviridae --Viruses
BIOSIS Concept Code(s)- 00520; 02506; 02508; 10063; 10069; 13202; 15002; 15004; 25000; 33506; 34502; 34508; 36006; 37052; 37054; 37056
BIOSYSTEMATIC CODES- 02623; 86215
CAS REGISTRY/EC NUMBER(S)- *1406-18-4 --VITAMIN E; *7440-66-6 --ZINC
CONCEPT CODE(S)- Orlando, Florida, USA
CHEMICAL INDEXING- print .

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7. Improvement of immune functions in HIV infection by sulfur supplementation: Two randomized trials .
BIO 03-20 03-170415 NDN- 199-0046-0153-4

Droege, Wulf; Beichert, Matthias; Breitkreutz, Raoul; Brust, Juergen; Daniel, Volker; Edler, Lutz; Hack, Volker; Nebe, Carl Thomas; Pittack, Nicole; Schuster, Dieter

JOURNAL NAME- Journal of Molecular Medicine (Berlin).
VOL. 78
NO. 1
2000
PP. 55-62.
DOCUMENT TYPE- Article
ISSN- 0946-2716
ADDRESS- Division of Immunochemistry, Deutsches Krebsforschungszentrum, Im Neuenheimer Feld 280, 69120, Heidelberg, Germany
LANGUAGE- ENGLISH

To determine the therapeutic effect of sulfur amino acid supplementation in HIV infection we randomized 40 patients with antiretroviral therapy (ART; study 1) and 29 patients without ART (study 2) to treatment for 7 months with N-acetyl-cysteine or placebo at an individually adjusted dose according to a defined scheme. The main outcome measures were the change in immunological parameters including natural killer (NK) cell and T cell functions and the viral load. Both studies showed consistently that N-acetyl-cysteine causes a marked increase in immunological functions and plasma albumin concentrations. The effect of N-acetyl-cysteine on the viral load, in contrast, was not consistent and may warrant further studies. Our findings suggest that the impairment of immunological functions in HIV+ patients results at least partly from cysteine deficiency. Because immune reconstitution is a widely accepted aim of HIV treatment, N-acetyl-cysteine treatment may be recommended for patients with and without ART. Our previous report on the massive loss of sulfur in HIV-infected subjects and the present demonstration of the immunoreconstituting effect of cysteine supplementation indicate that the HIV-induced cysteine depletion is a novel mechanism by which a virus destroys the immune defense of the host and escapes immune elimination.

DESCRIPTOR(S)- *Clinical Immunology (Human Medicine, Medical Sciences); *Infection; *Pharmacology; *human (Hominidae) --patient; * human immunodeficiency virus HIV (Retroviridae) --pathogen; *Animal Viruses; *Animals; *Chordates; *Humans; *Mammals;

*Microorganisms; *Primates; *Vertebrates; *Viruses; *natural killer cells --blood and lymphatics; *natural killer cells --function; *natural killer cells --immune system; *T cells --blood and lymphatics; *T cells --function; *T cells --immune system; *cysteine deficiency --nutritional disease; * human immunodeficiency virus infection HIV infection --immune system disease; * human immunodeficiency virus infection HIV infection --viral disease; *N-acetyl-cysteine --replenishing agent-drug; *antiretroviral therapy --therapeutic method; * sulfur amino acid supplementation --supplementation method; * sulfur amino acid supplementation --therapeutic effect; *immune functions; *viral load; *HIV Infections (MeSH)
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Hominidae --Animalia; Hominidae --Chordata; Hominidae --Mammalia; Hominidae --Primates; Hominidae --Vertebrata; Retroviridae --Animal Viruses; Retroviridae --Microorganisms; Retroviridae --Viruses
BIOSIS Concept Code(s)- 12512; 13203; 15002; 22005; 22008; 33506; 34502; 34508; 36006
BIOSYSTEMATIC CODES- 02623; 86215
CAS REGISTRY/EC NUMBER(S)- *616-91-1 --N-ACETYL-CYSTEINE .

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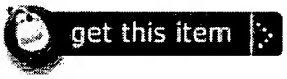
8. Neuropsychological performance in relationship to selenium status in the Miami HIV-1 infected drug abusers (MIDAS) study .
BIO 03-08 03-064192 NDN- 199-0035-3930-4



Zhang, G.; Wilkie, F.; Shor-Posner, G.; Quesada, J.; Miguez, M.; Lecusay, R.; Lai, S.; Garcia, R.; Campa, A.; Baum, M. K. .

JOURNAL NAME- Society for Neuroscience Abstracts.
VOL. 25.
NO. 1-2.
1999.
PP. 43..
DOCUMENT TYPE- Meeting.
ISSN- 0190-5295.
ADDRESS- Depts of Psychiatry and Behavioral Sciences, and Medicine, Univ of Miami School of Medicine, Miami, FL., USA.
SPONSOR- The Society for Neuroscience.
CONFERENCE DATE- October 23-28, 1999.
CONFERENCE TITLE- 29th Annual Meeting of the Society for Neuroscience, Part 1.

NO-ABSTRACT

DESCRIPTOR(S)- *Infection; *Nervous System (Neural Coordination).; *human (Hominidae) --drug abusers.; *HIV-1 human immunodeficiency virus 1 (Retroviridae) --pathogen; *Animal Viruses; *Animals; *Chordates; *Humans; *Mammals; *Microorganisms; *Primates; *Vertebrates; *Viruses.; *brain --nervous system.; *HIV-1 infection human immunodeficiency virus 1 infection --immune system disease; *HIV-1 infection human immunodeficiency virus 1 infection --viral disease.; * selenium --plasma.; * selenium therapy --therapeutic method.; *mental status; *neurophysical performance; *oxidative stress; *Meeting Abstract.; *MIDAS study ; *HIV

Infections (MeSH).
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Hominidae --Animalia; Hominidae --Chordata; Hominidae --Mammalia; Hominidae --Primates; Hominidae --Vertebrata; Retroviridae --Animal Viruses; Retroviridae --Microorganisms.; Retroviridae --Viruses
BIOSIS Concept Code(s)- 00520; 07003; 12512; 20501; 34502; 36001
BIOSYSTEMATIC CODES- 02623; 86215
CAS REGISTRY/EC NUMBER(S)- *7782-49-2 --SELENIUM.
CONCEPT CODE(S)- Miami Beach, Florida, USA. .

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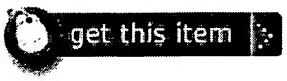
9. Effects of trace metal compounds on HIV-1 reverse transcriptase: An in vitro study .
BIO 02-27 02-270215 NDN- 199-0002-5178-4



Sabbioni, Enrico; Baricevic, Karla; Blanch, Neus; Serra, Miguel-Angel

JOURNAL NAME- Biological Trace Element Research
VOL. 68
NO. 2
May, 1999
PP. 107-120.
DOCUMENT TYPE- Article
ISSN- 0163-4984
ADDRESS- European Commission, Joint Research Centre-Ispra Site, Environment Institute, I-21020 Ispra, Varese, Italy
LANGUAGE- ENGLISH

The effect of 44 different metal ions (Ag+, Al3+, AsO2-, Au3+, Ba2+, Be2+, Bi3+, Cd2+, Ce3+, Co2+, CrO42-, Cr3+, Cs+, Cu2+, Fe3+, Fe2+, Ga3+, Ge4+, Hg2+, Ir4+, La3+, Li+, Mn2+, Mo6+, Ni2+, Os4+, Pb2+, Pt4+, Rb+, Rh3+, Sb5+, SeO42-, SeO32-, Sn2+, Sr2+, Th4+, Tl+, UO22+, VO3-, VO2+, WO42-, Y3+, Zn2+, and Zr4+) on the activity of the reverse transcriptase (RT) of the human immunodeficiency virus (HIV-1) was investigated in vitro. For this study, the RT activity assay was carried out by means of an enzyme-linked immunosorbent assay (ELISA) kit, using the template/primer hybrid poly(A) cntdot oligo(dT)15, which required some modifications: (1) possible interfering metal chelators (such as EDTA) in the original lysis buffer were avoided, and a new buffer (50 mM Tris-NO3, pH 7.8) was used throughout; (2) an amount of 2 ng of RT per well was considered to be optimal after checking the linearity of the reaction with increasing amounts of enzyme; (3) an incubation temperature of 37degreeC and an incubation time of 1 h were chosen after preliminary studies in a wide range of temperature and time. At an incubation temperature gtoreq40degreeC, there was a dramatic loss of enzymatic activity. In addition, when RT alone was preincubated for 1 h at 5degreeC, 25degreeC, and 37degreeC, there was a large (83%) loss of activity at 37degreeC as compared to that at 5degreeC. These results are indicative of enzyme thermolability, which is higher in the absence of substrates. The effect of metal ions on RT activity was tested using two different metal salt concentrations (10-4 M and 10-5 M). Under such experimental conditions, the presence of five metal ions (Pt4+, Ag+, Rh3+, Zn2+, and Hg2+) decreased the RT activity in a dose-response fashion. The observed order of effectiveness with respect to inhibition was Pt4+ >

Ag+ > Rh3+ > Zn2+ = Hg2+. Estimated mean inhibitory concentrations (IC50) were 7.8 muM for (NH4)2PtCl6, 14.1 muM for AgNO3, 46.8 muM for RhCl3, 53.7 muM for Zn(SO)4, and 56.2 muM for Hg(NO3)2. Because these data are of the same order of magnitude as the corresponding values related to other RT inhibitors used in anti-AIDS therapy, metal compounds or their derivatives could give an interesting contribution in the development of new RT inhibitors for clinical use.

DESCRIPTOR(S)- *Enzymology (Biochemistry and Molecular Biophysics); *Pharmacology; * human immunodeficiency virus 1 HIV-1 (Retroviridae) --pathogen; *Animal Viruses; *Microorganisms; *Viruses; *mercury ion; *platinum ion; *rhodium ion; *silver ion; *trace metal compounds; * zinc ion; *HIV-1 reverse transcriptase; *ELISA --detection method; *enzyme activity; *enzyme thermolability; *temperature; *time
BIOLOGICAL TAXONOMIC DESCRIPTOR(S)- Retroviridae --Animal Viruses; Retroviridae --Microorganisms; Retroviridae --Viruses
BIOSIS Concept Code(s)- 10050; 10060; 10802; 22002; 36001
BIOSYSTEMATIC CODES- 02623
CAS REGISTRY/EC NUMBER(S)- *14701-21-4 --SILVER ION; *23713-49-7 --ZINC ION; *7439-97-6 --MERCURY; *7440-06-4 --PLATINUM; *7440-16-6 --RHODIUM .

Citations from Federal Research in Progress (FRP): FRP

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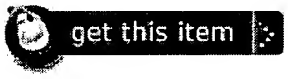
10. TRIALS OF VITAMINS IN HIV PROGRESSION AND TRANSMISSION
FRP 03-03 5R01HD32257-08 NDN- 049-0545-9172-9



FAWZI, WAFAIE W

AGENCY- CRISP
CORPORATE AUTHOR- HARVARD UNIVERSITY (SCH OF PUBLIC HLTH)
BOSTON
MASSACHUSETTS
SUPPORT ORGANIZATION NAME- NATIONAL INSTITUTE OF CHILD HEALTH AND HUMAN DEVELOPMENT
RESEARCHER ADDRESS- HARVARD SCH OF PUBLIC HEALTH, 665 HUNTINGTON AVE, BOSTON, MA 02115
AWARD TYPE- Noncompeting Continuation (Type 5)
FISCAL YEAR- 2001

During that last 4 years we screened 13,876 eligible Tanzanian pregnant women fo r HIV infection and enrolled and followed up 1085 consenting HIV-positive subjec ts. Women were randomized in a 2x2 factorial design to vitamin A alone, multivi tamins including vitamin A, multivitamins excluding vitamin A, or placebo. Labo ratory analyses to determine the effect of the supplements on vertical transmiss ion of HIV are ongoing. We examined the effect of the supplements on secondary endpoints for which data were complete (adverse pregnancy outcomes and T-cell su bsets). Women who received multivitamins experienced a significant and sustaine d increase in CD4 and CD8 cell

counts. We propose to continue following up mothe rs and children beyond the end date of field activities in the current cycle (1/ 31/1999). Given that CD4 and CD8 counts are far from perfect surrogate markers for disease progression, it is important to ascertain whether the supplements re sult in improvement in clinical condition or survival of patients. We also prop ose to follow up the children born to these mothers to prospectively examine the relationships between biochemical and dietary measures of vitamins A, E, B12, a nd selenium and progression to AIDS among infected children; and between these n utrients and morbidity (diarrheal disease and lower respiratory infections), gro wth retardation, and mortality among HIV infected and uninfected children. In pr eliminary analyses of the current study, we also observed substantial prevalence of HIV-1 subtypes, A, C, D, and recombinants. Limited data from other studies suggest that different HIV-1 subtypes may have different pathogenic potentials. We propose to expand the scope of work beyond our original nutritional aims to take advantage of a rare opportunity to examine if HIV-1 subtypes are associated with different rates of vertical transmission or with differential rates of dis ease progression, findings that are relevant for the design of vaccines. We hav e demonstrated during the first 4 years that the women in the study are prepared to participate in the proposed activities, that we can adhere to the research s chedule, maintain a high rate of follow up (our annual loss to follow up is only 6 percent), and can manage and analyze the data as it becomes available. Given the fast rate of disease progression among HIV- positive children and adults in developing countries, and the limited resources available to address this condi tion, low cost interventions including micronutrients and effective vaccines are urgently needed for developing countries.

DESCRIPTOR(S)- AFRICA; AIDS; AIDS EDUCATION /PREVENTION; AIDS THERAPY; CLINICAL RESEARCH; DIETARY SUPPLEMENT; HIV INFECTION; HUMAN PREGNANT SUBJECT; HUMAN THERAPY EVALUATION; INFANT HUMAN (0-1 YEAR); NUTRITION RELATED TAG; PEDIATRIC AIDS; RETINOID; SELENIUM ; TOCOPHEROL; VERTICAL TRANSMISSION; VIRUS CLASSIFICATION; VITAMIN B12; VITAMIN THERAPY .

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11. Zinc Therapy in Zinc Deficient HIV + Drug Users
FRP 03-03 1R01DA14966-01 NDN- 049-0543-9812-7

BAUM, MARIANNA K

AGENCY- CRISP
CORPORATE AUTHOR- FLORIDA INTERNATIONAL UNIVERSITY
MIAMI
FLORIDA
SUPPORT ORGANIZATION NAME- NATIONAL INSTITUTE ON DRUG ABUSE
RESEARCHER ADDRESS- FIU SCHOOL OF HEALTH, 11200 SW 8TH ST,UNIV PARK CH 2, MIAMI, FL 33199
AWARD TYPE- New Award (Type 1)
FISCAL YEAR- 2001

DESCRIPTION: Deficiency of zinc is prevalent in HAART and non-HAART treated HIV-1 seropositive males and female drug users and has been shown to have a profound impact on HIV

disease status. Low levels of zinc are associated with an increased risk for HIV-1 related mortality, while increasing levels of plasma zinc are associated with slower disease progression. Other investigators have reported that zinc administration in HIV/AIDS patients stabilized weight, increased CD4 cell count, and reduced the number of opportunistic infections. As drug users are particularly susceptible to zinc deficiency (56 percent have low serum zinc levels), zinc therapy in HIV-1 infected drug users with low zinc levels (> 0.35 ug/ml and < 0.75ug/ml), is both timely and warranted. Originally the proposal was to randomize 210 participants into the two study arms but the revised application intends to use stratified randomization based on viral load to balance any potential impact of antiretroviral treatment on CD4 cell count and clinical events. The investigators estimate that only 20 percent of the study population will be on newer therapies such as HAART. Zinc supplements will be given at nutritional doses (15 mg for men and 12 mg for women) and compliance to the intervention and safety will be monitored throughout the trial. Clinical and laboratory markers will be assessed at either 3 or 6 month intervals over the 30 month study.The specific aims will determine if zinc therapy in HIV-1 infected men and women who abuse drugs and have low plasma zinc levels will have higher CD4 cell counts, lower viral loads and prolonged time to events, including AIDS defining opportunistic infections, or AIDS-related death.

DESCRIPTOR(S)- AIDS THERAPY; ANTIAIDS AGENT; CLINICAL TRIAL ; DIET THERAPY; DIETARY SUPPLEMENT; HELPER T LYMPHOCYTE; HIV INFECTION; HUMAN IMMUNODEFICIENCY VIRUS 1; HUMAN MORTALITY; HUMAN SUBJECT; HUMAN THERAPY EVALUATION; INTERLEUKIN 2; INTRAVENOUS DRUG ABUSE; NUTRITION DISORDER; NUTRITION RELATED TAG; OPPORTUNISTIC INFECTION; PATIENT ORIENTED RESEARCH; THERAPY COMPLIANCE; VIREMIA; ZINC .

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12. NEUROPROTECTION WITH SELENIUM THERAPY IN HIV + IDUS
FRP 03-03 5R01DA12797-02 NDN- 049-0543-9063-3

SHOR-POSNER, GAIL

AGENCY- CRISP
CORPORATE AUTHOR- UNIVERSITY OF MIAMI
MIAMI
FLORIDA
SUPPORT ORGANIZATION NAME- NATIONAL INSTITUTE ON DRUG ABUSE
RESEARCHER ADDRESS- UNIVERSITY OF MIAMI, 1400 NW 10TH AVE, 6TH FLOOR, MIAMI, FL 33136
AWARD TYPE- Noncompeting Continuation (Type 5)
FISCAL YEAR- 2001

The major neuropsychiatric complication in HIV-disease is cognitive-motor impair ment, with HIV-1 seropositive drug users reported to be at higher risk for the d evelopment of HIV-associated dementia and more rapid progression in neurologic d isability. Oxidative stress, which can lead to neuronal degeneration, is increas ed in HIV-1 disease and appears to be potentiated by drugs of abuse. The primary objective of this ancillary study is to determine whether supplementation with selenium , a

biologic antioxidant that is required for protecting cells from oxid ative damage, can provide neuroprotection and help maintain cognitive function i n HIV-l seropositive chronic drug users. Supplementation with selenium has been shown to improve oxidative defense systems in HIV/AIDS patients, and inhibit men tal deterioration in neurologic patients. Our preliminary investigations in HIV- l infected drug users indicate that low levels of selenium are associated with decreased mental performance, and that short-term selenium supplementation resul ts in a strong potential for improvement in mental function and mood state. Thes e data suggest that administration of selenium may be an effective strategy to p revent loss of cognitive ability. We propose to extend our currently NIDA-funded , clinical trial, "Selenium Therapy to Slow Disease Progression in HIV+ IDUs", t o compare the effects of selenium or placebo on neuropsychological function. Con sented HIV-l infected drug users (n=120) will be enrolled at the baseline visit of the parent study, prior to supplementation, and administered a psychosocial a nd cognitive battery every 6 months for 30 months. Drug use, nutritional, immuno logic, oxidative stress, and health status data will be collected by the parent study at the same visit as the cognitive and psychosocial battery, and made avai lable for the proposed project. There is no direct scientific overlap between th e two studies. The proposed collaborative and cost-effective research provides a unique opportunity to further our understanding of neuropsychological function in HIV-l seropositive men and women who abuse drugs, as well as provide importan t information necessary for the management of cognitive impairment in HIV-1 dise ase.

DESCRIPTOR(S)- AIDS DEMENTIA COMPLEX; AIDS THERAPY; CHEMOPREVENTION; CLINICAL RESEARCH; CLINICAL TRIAL PHASE II /III /IV; COGNITION; DIET THERAPY; DIETARY MINERAL; DIETARY SUPPLEMENT; HIV INFECTION; HUMAN SUBJECT; INTRAVENOUS DRUG ABUSE; MENTAL DISORDER PREVENTION; NEURAL DEGENERATION; NEUROPROTECTANT; NEUROPSYCHOLOGICAL TEST; NEUROPSYCHOLOGY; NUTRITION RELATED TAG; OXIDATIVE STRESS; SELENIUM .

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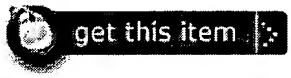
13. SELENIUM THERAPY TO SLOW HIV DISEASE PROGRESSION IN IDUS
FRP 03-03 5R01DA11378-04 NDN- 049-0543-8620-4



SHOR-POSNER, GAIL

AGENCY- CRISP
CORPORATE AUTHOR- UNIVERSITY OF MIAMI
MIAMI
FLORIDA
SUPPORT ORGANIZATION NAME- NATIONAL INSTITUTE ON DRUG ABUSE
RESEARCHER ADDRESS- UNIVERSITY OF MIAMI, 1400 NW 10TH AVENUE, MIAMI, FL 22136
AWARD TYPE- Noncompeting Continuation (Type 5)
FISCAL YEAR- 2001

DESCRIPTION: (Applicant's Abstract) The trace element, selenium , is essential for maintaining a viable and responsive immune system. Administered as a chemopreventive agent, it has been shown

to significantly reduce cancer mortality and be protective against a number of viral pathogens in a variety of clinical settings. Recent reports indicate that selenium is predictive of HIV-1 related prognosis, and may have an important role in preventing HIV-1 replication. Our studies in HIV-1 seropositive drug users demonstrate that selenium is a powerful predictor of HIV-1 disease progression and mortality. These compelling findings suggest that selenium administered as a chemopreventive agent may effectively modulate HIV disease progression. Our previous experience and a review of the literature indicate that selenium in nutritional doses is feasible and safe in HIV-1 infected individuals. The proposed study is a randomized, double-blind , controlled clinical trial comparing the effects of selenium or placebo in HIV-1 infected male and female drug users. A total of 328 HIV-1 infected adults will be randomized into the trial. At six month intervals, laboratory and clinical markers of disease progression will be evaluated, as well as selenium status, and specific drug use. Compliance to the intervention and potential toxicity will be monitored throughout the trial. This proposed investigation will permit us to determine whether supplemental selenium , as a chemopreventive agent, can enhance the immune system and reduce viral load to slow HIV-1 disease progression in male and female drug users.

DESCRIPTOR(S)- AIDS THERAPY; CHEMOPREVENTION; CLINICAL RESEARCH; CLINICAL TRIAL ; DRUG ABUSE; HIV INFECTION; HUMAN IMMUNODEFICIENCY VIRUS 1; HUMAN MORTALITY; HUMAN SUBJECT; HUMAN THERAPY EVALUATION; LONGITUDINAL HUMAN STUDY ; PATHOLOGIC PROCESS; PLACEBO; SELENIUM .

Citations from MEDLINE(R) DATABASE (2001 TO PRESENT): MED

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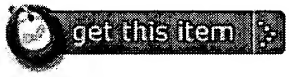
14. Diet survey and evaluation of ingested nutrients in a group of HIV patients
MED 03-13 22044664 NDN- 222-0367-0305-9



Izquierdo Villarroyal, B.; Celaya Perez, S.; Amiguet Garc.a, J. A.

JOURNAL NAME- Nutr Hosp
VOL. 17
2002 Mar-Apr
PP. 97-106
DOCUMENT TYPE- Journal Article
JOURNAL CODE- 9100365
JOURNAL SUBSET- MEDJSIM
ISSN- 0212-1611
CORPORATE AUTHOR- Servicio de Anestesiolog.a, Reanimacion y Terapia del Dolor, Hospital Miguel Servet, Espana. blizvi@comz.org
PUBLICATION COUNTRY- Spain
LANGUAGE- Spanish

OBJECTIVE: To study the relationship between nutritional status, immunological condition, clinical progress and food consumption in a group of patients infected with HIV. METHOD: Longitudinal

descriptive study of 30 HIV/AIDS patients. Anthropometric assessment (weight, height, skin folds, upper arm circumference). The intake of nutrients was calculated using a one-week dietary record. RESULTS: The mean amount of energy intake is 2,791 kcal with a 13.48% of protein, 40.12% of carbohydrates and 45.89% of lipids. The group of patients with weight loss presented a significantly greater proportion of proteins than group with normal weight. Patients with Kwashiorkor-like malnutrition presented an intake of proteins which was significantly lower than the group of well-nourished patients. The group of those whose nutritional status improved presented a significantly higher mean percentage of proteins in the diet than the other groups. CONCLUSIONS: The amount of the energy intake by patients is higher than that recommended. The diets show an excessive consumption of fats and a shortage of carbohydrates and proteins. Deficits are observed in vitamin B6 and vitamin E, magnesium and zinc . The increase in intake, by itself, does not improve the health status of the patients, indicating the need to provide them with the necessary dietary supplements from the early stages of their condition.

MEDICAL DESCRIPTOR(S)- *Diet; *Diet Surveys; *HIV Infections Adult; English Abstract; Female; Human; Longitudinal Studies ; Male
MESH Z TREE NUMBER(S)- E05.272; G06.696.384; E05.318.308.250.600.350; E05.318.308.585.550.350; G03.850.520.308.250.600.350; G03.850.520.308.585.550.350; N05.715.360.300.375.560.300; N05.715.360.300.560.565.300; C02.782.815.616.400; C02.800.801.400; C20.673.480 .

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15. Nutrient intake and body weight in a large HIV cohort that includes women and minorities.
MED 02-10 21834672 NDN- 222-0313-5613-8

Woods, M. N.; Spiegelman, D.; Knox, T. A.; Forrester, J. E.; Connors, J. L.; Skinner, S. C.; Silva, M.; Kim, J. H.; Gorbach, S. L.

JOURNAL NAME- J Am Diet Assoc
VOL. 102
2002 Feb
PP. 203-11
DOCUMENT TYPE- Journal Article
JOURNAL CODE- 7503061
JOURNAL SUBSET- MEDJSAIM; MEDJSIM
ISSN- 0002-8223
CORPORATE AUTHOR- Department of Family Medicine and Community Health, Tufts University School of Medicine, Boston, Mass 02111, USA. margo.wood@opal.tufts.edu
CONTRACT/GRANT NUMBER- DK4 5734-05.DK.NIDDK; M01-RR00054.RR.NCRR
PUBLICATION COUNTRY- United States
LANGUAGE- English

OBJECTIVE: Evaluate the baseline nutrient intake of an HIV positive population that includes significant representation from women and minorities, and determine the relationship between state

of disease and nutritional intake. DESIGN: Baseline data from a prospective study (Nutrition for Healthy Living). SUBJECTS: Individuals with HIV in the Boston and Rhode Island area (n = 516); 25% were women and 30% were minorities. METHODS: Nutrient intakes from 3-day food records, which included vitamin/mineral supplements, were estimated by gender and nonwhite vs white categories, after grouping by CD4 lymphocyte counts. STATISTICAL ANALYSES: Spearman correlation coefficients, Wilcoxon signed rank test, Wilcoxon rank sum test, chi2 test, and restricted cubic spline model were used for data analyses as indicated. RESULTS: Macronutrient but not micronutrient intake was statistically and inversely associated with decreasing CD4 cell counts. The median intake of micronutrients was higher in the study sample compared with the same age and gender group in NHANES III data; however, 25% to 35% of the women in our study sample had dietary intakes of less than 75% of the DRIs for vitamins A, C, E and B-6, and iron and zinc . White men had statistically higher values of all micronutrients compared with nonwhite men. Body mass index for men and women ranged from 23 to 25. CONCLUSIONS/APPLICATIONS: Median values for micronutrient intake from food plus vitamin/mineral supplements were adequate in the overall population studied, but a large percent of women and minorities had inadequate nutrient intakes and would benefit from dietary assessment and counseling.

MEDICAL DESCRIPTOR(S)- *Body Weight; *Energy Intake--PH; *HIV Infections --PP; *Minerals --AD; *Vitamins --AD Adult; CD4 Lymphocyte Count; Cohort Studies ; Diet Records; Dietary Carbohydrates --AD; Dietary Fats--AD; Dietary Proteins --AD; Female; Human; Male; Minerals --BL; Minority Groups; Nutrition Assessment; Prospective Studies ; Statistics, Nonparametric; Support, U.S. Gov't, P.H.S.; Vitamins --BL
CAS SUBSTANCE NAME(S)- Dietary Carbohydrates; Dietary Fats; Dietary Proteins; Minerals; Vitamins
MESH Z TREE NUMBER(S)- E01.370.600.110.120; E05.118.090.287; G07.553.481.398; G06.696.384.250; C02.782.815.616.400; C02.800.801.400; C20.673.480; D01.578; D11.786 .

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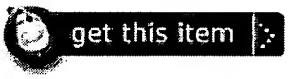
16. Vitamin A supplements ameliorate the adverse effect of HIV-1, malaria, and diarrheal infections on child growth.
MED 02-08 21635860 NDN- 222-0312-2689-9



Villamor, E.; Mbise, R.; Spiegelman, D.; Hertzmark, E.; Fataki, M.; Peterson, K. E.; Ndossi, G.; Fawzi, W. W.

JOURNAL NAME- Pediatrics
VOL. 109
2002 Jan
PP. E6
DOCUMENT TYPE- Clinical Trial; Journal Article; Randomized Controlled Trial
JOURNAL CODE- 0376422
JOURNAL SUBSET- MEDJSAIM; MEDJSIM
ISSN- 1098-4275
CORPORATE AUTHOR- Department of Nutrition, Harvard School of Public Health, Boston, Massachusetts. Department of Epidemiology, Harvard School of Public Health, Boston,

Massachusetts, USA. evillamo@hsph.harvard.edu
PUBLICATION COUNTRY- United States
LANGUAGE- English

OBJECTIVE: Evidence from animal experiments and observational studies in humans suggests that vitamin A plays a fundamental role in physical growth. However, results from vitamin A supplementation trials in children are inconsistent; whereas some did not find an overall effect on growth, others found benefits only among specific groups, including children with low concentrations of serum retinol or short duration of breastfeeding. The apparent lack of an overall effect of vitamin A on growth could be attributed to context-specific distribution of conditions that affect both growth and the response to supplementation, eg, baseline vitamin A status, deficiency of other nutrients (fat, zinc), and the presence of infectious diseases. Human immunodeficiency virus (HIV) infection, malaria, and diarrheal disease adversely affect growth and are associated with increased prevalence of vitamin A deficiency. We hypothesize that vitamin A supplementation could ameliorate the adverse effect of these infections on child growth. METHODS: We conducted a randomized, clinical trial among 687 Tanzanian children who were 6 to 60 months of age and admitted to the hospital with pneumonia. Children were assigned to oral doses of 200 000 IU vitamin A (half that dose if 6012 months) or placebo on the day of admission, a second dose on the following day, and third and fourth doses at 4 and 8 months after discharge from the hospital, respectively. Anthropometric measurements were obtained at baseline and at monthly visits to the study clinics during 12 months after the initial hospitalization. Surveillance on the incidence and severity of diarrhea and respiratory infections was conducted during biweekly visits, alternately at a study clinic and the child's home, using a pictorial diary that the mothers were trained to use. A blood specimen was drawn at baseline for determination of HIV status, malaria infection, and hemoglobin levels. We used mixed effects models to compare estimated total weight and height increases after 1 year of follow-up between treatment arms, overall and within levels of HIV status, malaria, and other possible baseline effect modifiers. We also assessed the potential modulating effect of vitamin A on the risk of stunting (height-for-age 60-2 standard deviations of the gender-specific National Center for Health Statistics median reference) attributable to diarrheal and respiratory infections during follow-up, in the subset of children who were not stunted at baseline. A similar approach was followed for wasting (weight-for-height 60-2 standard deviations of the reference median). Cox regression models were used to estimate relative risks and 95% confidence intervals (CI), treating episodes of infection as time-dependent covariates. RESULTS: A total of 554 children had at least 2 follow-up measurements of height or weight and constituted the study base. Baseline characteristics did not differ significantly by treatment arm. Seventy-three percent of the children were 602 years of age, and 37% were 6012 months; 31% were stunted at baseline and 9% were wasted. Malaria (Plasmodium falciparum) and HIV infection were found in 24% and 9% of the children, respectively. Median duration of follow-up was 351 days, with 10 measurements/child, on average, irrespectively of treatment assignment. Supplementation with vitamin A among children who had HIV infection and were 6018 months of age resulted in a significant length increase. Four months after the first dose, infants who were HIV positive in the vitamin A arm had gained, on average, 2.8 cm (95% CI: 1.0-4.6) more than children who received placebo, whereas no effect was observed among infants who were HIV negative (difference at 4 months: -0.2 cm; 95% CI: -0.8-0.5). Children who were 6012 months of age and had malaria at enrollment experienced a 747-g (95% CI: 71-1423) higher yearly weight gain attributable to vitamin A; among children without malaria, however, the supplements did not have a significant effect (-57 g; 95% CI: -461-348). These results remained unchanged after controlling for indicators of the socioeconomic and nutritional status at baseline. Linear growth was also improved by vitamin A among children from households with poor water supply (0.8 cm/year; 95% CI: 0-1.5) but not in children with tap water in the house or compound (-1.0 cm/year; 95% CI: -1.9-0). Weight gain was greater among children with mid-upper arm

circumference below the 25th percentile of the age-specific distribution at baseline (458 g/year; 95% CI: 1-905), but no benefit was evident among children with higher mid-upper arm circumference. The risk of stunting associated with episodes of persistent diarrhea (lasting 14 or more days) during follow-up was virtually eliminated by vitamin A supplements. Among children in the placebo group, the average risk of stunting associated with 1 or more episodes of persistent diarrhea between 2 consecutive visits was 5.2 times higher (95% CI: 2.4-11.2) than that of children without diarrhea or with acute episodes. In contrast, among children who received vitamin A, there was virtually no risk of stunting associated with persistent diarrhea (relative risk: 1.0; 95% CI: 0.3-1.3). This effect was slightly attenuated after controlling for the number of household possessions, gender, baseline low arm circumference, HIV infection, and presence of malaria parasites in blood. Vitamin A supplements did not modify the associations between respiratory infections and the risk of stunting or wasting. CONCLUSIONS: Vitamin A supplementation improves linear and ponderal growth in infants who are infected with HIV and malaria, respectively, and decreases the risk of stunting associated with persistent diarrhea. Supplementation could constitute a low-cost, effective intervention to decrease the burden of growth retardation in settings where infectious diseases are highly prevalent.

MEDICAL DESCRIPTOR(S)- *Acquired Immunodeficiency Syndrome --CO; *Diarrhea --CO; *Growth Disorders --PC; *Malaria --CO; *Vitamin A --AD Body Height; Body Weight; Child, Preschool; Dietary Supplements; Double-Blind Method; Female; Follow-Up Studies ; Growth Disorders --ET; Human; Infant; Male; Support, Non-U.S. Gov't
CAS REGISTRY/EC NUMBER(S)- *11103-57-4
CAS SUBSTANCE NAME(S)- Vitamin A
MESH Z TREE NUMBER(S)- C02.782.815.616.400.040; C02.800.801.400.040; C02.839.040; C20.673.480.040; C06.405.469.237; C23.888.821.214; C23.550.393; C03.752.250.552; D02.455.849.291.700.818; D11.557.261.700.860; D11.786.652 .

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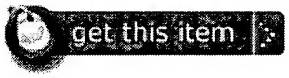
17. Micronutrients and child health: studies in international nutrition and HIV infection.
MED 02-01 21577364 NDN- 222-0303-3960-1



Duggan, C.; Fawzi, W.

JOURNAL NAME- Nutr Rev
VOL. 59
NO. 11
2001 Nov
PP. 358-69
161 reference(s)
DOCUMENT TYPE- Journal Article; Review; Review, Tutorial
JOURNAL CODE- 0376405
JOURNAL SUBSET- MEDJSIM
ISSN- 0029-6643
CORPORATE AUTHOR- Department of Pediatrics, Harvard Medical School, Boston, MA 02115, USA.

CONTRACT/GRANT NUMBER- D43 TW00004.TW.FIC; D43 TW01265.TW.FIC; P30-DK40561.DK.NIDDK; R01 32257.PHS; U01 45441.PHS
PUBLICATION COUNTRY- United States
LANGUAGE- English

Increasing data link micronutrient deficiencies to excess childhood morbidity and mortality, and similar relationships have been noted in the study of nutrition and HIV infection. We review epidemiologic studies that have examined the relationship between micronutrient deficiencies and health outcomes in childhood and HIV infection, as well as clinical trials of micronutrient supplementation. Vitamin A supplementation among communities at risk of deficiency effectively reduces mortality and morbidity in children younger than age 5, and vitamin A may be especially effective in HIV-infected children. Vertical transmission of HIV has not to date been affected by maternal micronutrient supplementation. In children with poor dietary zinc intake and/or bioavailability, zinc supplementation reduces the incidence and severity of diarrheal diseases, as well as the occurrence of pneumonia. Vitamin A therapy has not been associated with improved growth, whereas some trials have shown that zinc supplementation is associated with greater increments in height. Further trials of micronutrient supplementation are warranted.

MEDICAL DESCRIPTOR(S)- *HIV Infections --DT; *Micronutrients --AD; *Micronutrients --DF; *Nutrition Disorders --DT Child; Child, Preschool; Dietary Supplements; Disease Transmission, Vertical --PC; Female; HIV Infections -- MO; HIV Infections --TM; Human; Infant; Infant, Newborn; Male; Morbidity; Nutrition Disorders -- MO; Pregnancy; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.; Treatment Outcome; Vitamin A --AD; Vitamin A Deficiency --DT; Vitamin A Deficiency --EP; Zinc --AD; Zinc --DF
CAS REGISTRY/EC NUMBER(S)- *11103-57-4; *7440-66-6
CAS SUBSTANCE NAME(S)- Micronutrients; Vitamin A; Zinc .

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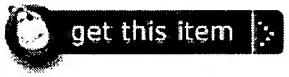
18. Structure of the human zinc finger protein HIVEP3: molecular cloning, expression, exon-intron structure, and comparison with paralogous genes HIVEP1 and HIVEP2.
MED 01-08 21100880 NDN- 222-0235-3723-1



Hicar, M. D.; Liu, Y.; Allen, C. E.; Wu, L. C.

JOURNAL NAME- Genomics
VOL. 71
2001 Jan 1
PP. 89-100
DOCUMENT TYPE- Journal Article
JOURNAL CODE- GEN; 8800135
JOURNAL SUBSET- MEDJSIM
ISSN- 0888-7543
CORPORATE AUTHOR- Department of Molecular Virology, Immunology, and Medical Genetics, College of Medicine and Public Health, The Ohio State University, Columbus, Ohio 43210, USA.

CONTRACT/GRANT NUMBER- GM48798.GM.NIGMS; P30 CA16058.CA.NCI
PUBLICATION COUNTRY- United States
LANGUAGE- English

Here we report the cloning and characterization of HIVEP3, the newest member in the human immunodeficiency virus type 1 enhancer-binding protein family that encodes large zinc finger proteins and regulates transcription via the kappaB enhancer motif. The largest open reading frame of HIVEP3 contains 2406 aa. and is approximately 80% identical to the mouse counterpart. The HIVEP3 gene is located in the chromosomal region 1p34 and is at least 300 kb with 10 exons. RNA studies show that multiple HIVEP3 transcripts are differentially expressed and regulated. Additionally, transcription termination occurs in the ultimate exon, exon 10, or in exon 6. Therefore, HIVEP3 may produce protein isoforms that contain or exclude the carboxyl DNA binding domain and the leucine zipper by alternative RNA splicing and differential polyadenylation. Sequence homologous to HIVEP3 exon 6 is not found in mouse nor are the paralogous genes HIVEP1 and HIVEP2. Zoo-blot analysis suggests that sequences homologous to the human exon 6 are present only in primates and cow. Therefore, a foreign DNA harboring a termination exon likely was inserted into the HIVEP3 locus relatively recently in evolution, resulting in the acquisition of novel gene regulatory mechanisms as well as the generation of structural and functional diversity. Copyright 2001 Academic Press.

MEDICAL DESCRIPTOR(S)- *Carrier Proteins --CH; *DNA-Binding Proteins --CH; *DNA-Binding Proteins --GE Amino Acid Sequence; Animal; Blotting, Northern; Blotting, Southern; Brain --ME; Carrier Proteins --GE; Chromosomes, Human, Pair 1; Cloning, Molecular; Comparative Study ; Cosmids; DNA, Complementary --ME; DNA-Binding Proteins --BI; Exons; Expressed Sequence Tags; Gene Library; Human; Introns; Mice; Models, Genetic; Molecular Sequence Data; Oligonucleotide Probes --ME; Open Reading Frames; Phylogeny; Poly A --ME; Protein Isoforms; Protein Structure, Tertiary; Reverse Transcriptase Polymerase Chain Reaction; Sequence Homology, Amino Acid; Support, U.S. Gov't, P.H.S.; Tissue Distribution; Transcription, Genetic; Zinc Fingers

CAS REGISTRY/EC NUMBER(S)- *138930-35-5; *24937-83-5
CAS SUBSTANCE NAME(S)- Carrier Proteins; Cosmids; DNA, Complementary; DNA-Binding Proteins; HIV-enhancer binding protein EP3; Oligonucleotide Probes; PRDII-BF1 protein; Protein Isoforms; HIV-enhancer binding protein EP2; Poly A .

Citations from MEDLINE(R) DATABASE (1997 TO 2000): ME1

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19. Status of selected nutrients and progression of human immunodeficiency virus type 1 infection.
MED 00-12 20424619 NDN- 194-0189-3024-1

Bogden, J. D.; Kemp, F. W.; Han, S.; Li, W.; Bruening, K.; Denny, T.; Oleske, J. M.; Lloyd, J.; Baker, H.; Perez, G.; Kloser, P.; Skurnick, J.; Louria, D. B.

JOURNAL NAME- Am J Clin Nutr
VOL. 72
NO. 3
2000 Sep
PP. 809-15
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- 3EY
JOURNAL SUBSET- MEDJSM; MEDJSA
ISSN- 0002-9165
CORPORATE AUTHOR- Department of Preventive Medicine and Community Health, the University of Medicine and Dentistry of New Jersey-New Jersey Medical School, Newark. bogden@umdnj.edu
CONTRACT/GRANT NUMBER- AI-95013.AI.NIAID
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

BACKGROUND: Immune function is highly dependent on nutritional status because the large mass and high rate of cellular turnover of the immune system make it a major user of nutrients. Furthermore, nutrient requirements may be increased during acute and chronic infections, including HIV-1 infection. OBJECTIVE: The current study was designed to assess relations among HIV-1 progression and 11 nutritional and demographic variables. DESIGN: The participants were 106 HIV-infected outpatients and 29 uninfected control subjects (n = 89 men and 46 women; age range: 35-57 y). The HIV-infected subjects represented a broad range of disease progression. RESULTS: We found lower concentrations of plasma and erythrocyte magnesium and of erythrocyte reduced glutathione beginning early in the course of HIV-1 infection. Significantly decreased hematocrit and increased serum copper concentration developed only late in the course of the disease. Statistically significant univariate associations were found between the CD4(+) T lymphocyte count and hematocrit, plasma magnesium concentration, and plasma zinc concentration. The lowest erythrocyte magnesium concentrations occurred in HIV-infected subjects who consumed alcoholic beverages. Independent variables that were significant joint predictors of CD4(+) cell count in multiple regression analyses were hematocrit and plasma free choline and zinc concentrations. These 3 factors together explained 43% of the variability in CD4(+) cell counts. CONCLUSION: The results provide evidence that compromised nutritional and antioxidant status begin early in the course of HIV-1 infection and may contribute to disease progression.

MEDICAL DESCRIPTOR(S)- *HIV Infections --PP; *HIV-1; *Nutrition Adult; Alcohol Drinking; Anti-HIV Agents --TU; Cross-Sectional Studies ; CD4 Lymphocyte Count; Disease Progression; Female; Human; HIV Infections --BL; HIV Infections--DT; Male; Middle Age; Reference Values; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
CAS REGISTRY/EC NUMBER(S)- *0
CAS SUBSTANCE NAME(S)- Anti-HIV Agents .

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20. Improvement of immune functions in HIV infection by sulfur supplementation: two randomized trials Ýsee comments"
MED 00-08 20220780 NDN- 194-0175-3123-5

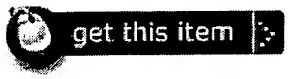
Breitkreutz, R.; Pittack, N.; Nebe, C. T.; Schuster, D.; Brust, J.; Beichert, M.; Hack, V.; Daniel, V.; Edler, L.; Droge, W.

JOURNAL NAME- J Mol Med
VOL. 78
NO. 1
2000
PP. 55-62
DOCUMENT TYPE- CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL
JOURNAL CODE- B8C
JOURNAL SUBSET- MEDJSM
ISSN- 0946-2716
CORPORATE AUTHOR- Deutsches Krebsforschungszentrum, Division of Immunochemistry, Heidelberg, Germany.
COMMENTS IN- Comment in:, J Mol Med, 2000 ;78(1):1-2
PUBLICATION COUNTRY- GERMANY
LANGUAGE- English

To determine the therapeutic effect of sulfur amino acid supplementation in HIV infection we randomized 40 patients with antiretroviral therapy (ART; study 1) and 29 patients without ART (study 2) to treatment for 7 months with N-acetyl-cysteine or placebo at an individually adjusted dose according to a defined scheme. The main outcome measures were the change in immunological parameters including natural killer (NK) cell and T cell functions and the viral load. Both studies showed consistently that N-acetyl-cysteine causes a marked increase in immunological functions and plasma albumin concentrations. The effect of N-acetyl-cysteine on the viral load, in contrast, was not consistent and may warrant further studies. Our findings suggest that the impairment of immunological functions in HIV+ patients results at least partly from cysteine deficiency. Because immune reconstitution is a widely accepted aim of HIV treatment, N-acetyl-cysteine treatment may be recommended for patients with and without ART. Our previous report on the massive loss of sulfur in HIV-infected subjects and the present demonstration of the immunoreconstituting effect of cysteine supplementation indicate that the HIV-induced cysteine depletion is a novel mechanism by which a virus destroys the immune defense of the host and escapes immune elimination.

CHECK TAG(S)- Female; Human; Male
MEDICAL DESCRIPTOR(S)- *Acetylcysteine --TU; *Acquired Immunodeficiency Syndrome --DT; *HIV-1 Acetylcysteine --AD; Acquired Immunodeficiency Syndrome --BL; Acquired Immunodeficiency Syndrome --IM; Acquired Immunodeficiency Syndrome --VI; Administration, Oral; Adolescence; Adult; Antigens, CD --ME; Double-Blind Method; Glutamine --BL; Interleukin-6 --BL; Killer Cells, Natural --ME; Middle Age; Placebos; Serum Albumin --ME; T-Lymphocytes --ME; Thioredoxin --BL; Viral Load
CAS REGISTRY/EC NUMBER(S)- *0; *0; *0; *0; *52500-60-4; *56-85-9; *616-91-1
CAS SUBSTANCE NAME(S)- Antigens, CD; Interleukin-6; Placebos; Serum Albumin; Thioredoxin; Glutamine; Acetylcysteine .

21. A recent study shows selenium supplementation benefits HIV patients: Selenomax decreases risk of development of depressed-dejected mood state Ýnews¨
MED 00-07 20215514 NDN- 194-0173-8388-0



NO-AUTHOR

JOURNAL NAME- J Assoc Nurses AIDS Care
VOL. 11
NO. 2
2000 Mar-Apr
PP. 103
DOCUMENT TYPE- NEWS
JOURNAL CODE- A7P
JOURNAL SUBSET- MEDJSM; MEDJSN
ISSN- 1055-3290
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

NO-ABSTRACT

CHECK TAG(S)- Female; Human; Male
MEDICAL DESCRIPTOR(S)- *Depression --DT; *Depression --VI; *HIV Infections --PX; *HIV-1; * Selenium --TU
CAS REGISTRY/EC NUMBER(S)- *7782-49-2
CAS SUBSTANCE NAME(S)- Selenium .

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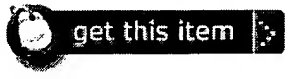
22. Development of an instrument to assess nutritional risk factors for children infected with human immunodeficiency virus.
MED 00-05 20184320 NDN- 194-0166-6594-3



Heller, L.; Fox, S.; Hell, K. J.; Church, J. A.

JOURNAL NAME- J Am Diet Assoc
VOL. 100
NO. 3
2000 Mar
PP. 323-9
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- H6F

JOURNAL SUBSET- MEDJSA; MEDJSM
ISSN- 0002-8223
CORPORATE AUTHOR- Division of Clinical Immunology and Allergy, Childrens Hospital of Los Angeles, University of Southern California School of Medicine, USA.
CONTRACT/GRANT NUMBER- NHLBI 38633-06; MOIRR00240
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

OBJECTIVE: To produce a simple and effective instrument to evaluate and monitor the nutritional risk of children infected with the human immunodeficiency virus (HIV). DESIGN: The test instrument was developed in consultation with 5 physicians, 5 nutritionists, and 5 social workers with expertise in caring for HIV-infected children. Patient information was collected through medical record review for 19 sociodemographic, 10 anthropometric, 4 biochemical, 6 dietary intake, and 19 medical factors. As a part of routine nutrition care, anthropometric data were obtained and the caregiver was asked to complete a 3-day diet record. Also recorded were the most recent CD4+ T-cell numbers and serum HIV p24 antigen and plasma HIV RNA levels. SUBJECTS/SETTING: Thirty-nine HIV-infected children were selected using quota sampling; that is, subjects were stratified by clinical class as defined by the Centers for Disease Control and Prevention. STATISTICAL ANALYSIS: The severity or degree of potential nutritional risk in each section (anthropometric, biochemical, dietary intake, and medical data) was graded (0 to 4, 0 = low risk) and summed. Reliability of internal consistency was determined through covariance matrixes. Validity was determined through Pearson product moment correlation coefficients to measure convergent and divergent validity; predictive validity was determined using analysis of variance. Correlation for validity was compared to 6 selected dependent variables: weight for height, weight growth velocity, lean body mass, serum albumin level, CD4+ T-cell numbers, and quantitative plasma HIV RNA levels. RESULTS: Of the 38 factors that were analyzed for reliability, 11 fell in the strongly reliable range: height for age, weight for age, clinical class, somatic protein stores, mid-arm circumference, weight for height, serum albumin, immunologic status, body mass index, energy intake, and opportunistic infection. CONCLUSIONS: Anthropometric, dietary intake, and medical data were reliable indicators of nutritional risk. The entire instrument was reliable after 8 of the weakest items were removed. The instrument was found to be valid and a good predictor of nutritional risk in HIV-infected children.

CHECK TAG(S)- Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
MEDICAL DESCRIPTOR(S)- *Diet; *HIV Infections --PP; *Nutrition Disorders --ET Adolescence; Anthropometry; Child; Child, Preschool; Cross-Sectional Studies ; Diet Records; Dietary Proteins --AD; Energy Intake; HIV Infections --CO; Infant; Iron --BL; Medical Records; Nutrition Disorders --EP; Nutrition Policy; Prealbumin --AN; Reproducibility of Results; Risk Factors; Serum Albumin --AN; Zinc --BL
CAS REGISTRY/EC NUMBER(S)- *0; *0; *0; *7439-89-6; *7440-66-6
CAS SUBSTANCE NAME(S)- Dietary Proteins; Prealbumin; Serum Albumin; Iron; Zinc .

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23. Contribution of zinc to reduce CD4+ risk factor for 'severe' infection relapse in aging: parallelism with HIV .
MED 99-10 99335120 NDN- 194-0140-9182-0

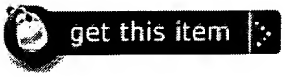
Mocchegiani, E.; Muzzioli, M.; Gaetti, R.; Veccia, S.; Viticchi, C.; Scalise, G.

JOURNAL NAME- Int J Immunopharmacol
VOL. 21
NO. 4
1999 Apr
PP. 271-81
DOCUMENT TYPE- CLINICAL TRIAL; CONTROLLED CLINICAL TRIAL; JOURNAL ARTICLE
JOURNAL CODE- GRI
JOURNAL SUBSET- MEDJSM
ISSN- 0192-0561
CORPORATE AUTHOR- Immunology Centre, Gerontol, Res. Dept., N. Masera, Italian National Research Centres on Aging, Ancona. e.mocchegiani@inrca.it
PUBLICATION COUNTRY- ENGLAND
LANGUAGE- English

Aging and HIV have parallelism in immunodeficiency status because of the appearance of infections or relapse leading to death in both conditions. HIV-RNA is predictor for HIV progression correlated with CD4+ depletion. CD4+ and plasma zinc levels (zincaemia) may be predictors for infections relapse in aging because of zinc relevance for normal immune efficiency against infections and for CD4+ growth. Moreover, zincaemia decreases in aging and infection. A total of 67 elderly subjects affected by infections resistant to antibiotic therapy were recruited. A total of 28 HIV+ subjects with HAART therapy were also used. CD4+ depletion (507 mm3) and zincaemia deficiency (76 microg/dl), as compared to CD4+ (700-1100 mm3) and zincaemia (85-100 microg/dl; age 40-75 years) normal ranges, are possible limits (Cox hazard regression) for severe infections relapse, such as chronic obstructive bronchitis and bronchopneumonia by bacteria or Candida complication, in aging. CD4+ and zincaemia values are within the lower limits of normal range in urinary tract infections. Zincaemia and HIV-RNA or CD4+ are inversely correlated ($r = 0.57$ and $r = 0.72$, respectively) in HIV+ HAART treated subjects. Consequently there is no appearance of opportunistic infections. Parallelism between aging and HIV may exist because of the resemblance in marked zinc deficiency and CD4+ depletion with high scores in relative risks for severe infections relapse. Supplementing zinc (12 mg Zn++/day) for one month in infected elderly subjects and HAART therapy in HIV+ subjects reduces risk scores in CD4+ and zincaemia deficiencies for infections relapse, suggesting that the zinc beneficial effect may be independent either by HIV-virus or pathogen agents involved. While HAART may reduce the occurrence of opportunistic infections in HIV by means of also major zinc bioavailability, supplementing zinc can be recommended in elderly people as resistance to infections. Since zinc deficiency is correlated with CD4+ depletion, this latter may also be good diagnostic marker to detect 'clear immunodeficiency' in aging, as in HIV condition.

CHECK TAG(S)- Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
MEDICAL DESCRIPTOR(S)- *Aging --IM; *HIV Infections --IM; * Zinc --IM; * Zinc --TU Adult; Aged; Double-Blind Method; HIV Infections --BL; HIV Infections --DT; Middle Age; Retrospective Studies ; Risk Factors; Zinc --BL; Zinc --DF
CAS REGISTRY/EC NUMBER(S)- *7440-66-6
CAS SUBSTANCE NAME(S)- Zinc .

24. Hypocalcaemia in HIV infection and AIDS.
MED 99-06 99195523 NDN- 194-0123-8149-1



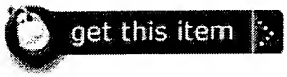
Kuehn, E. W.; Anders, H. J.; Bogner, J. R.; Obermaier, J.; Goebel, F. D.; Schlondorff, D.

JOURNAL NAME- J Intern Med
VOL. 245
NO. 1
1999 Jan
PP. 69-73
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- I2G
JOURNAL SUBSET- MEDJSM; MEDJSX
ISSN- 0954-6820
CORPORATE AUTHOR- Medizinische Poliklinik, Ludwig Maximilians University Munchen, Germany. anneli.ivarsson@epiph.umu.se
PUBLICATION COUNTRY- ENGLAND
LANGUAGE- English

OBJECTIVES: To study the prevalence and possible mechanisms of hypocalcaemia in HIV infection and AIDS. SUBJECTS: 828 patients with HIV infection or AIDS and 549 controls. INTERVENTIONS: Measurements of total serum calcium and albumin levels. Parameters of calcium homeostatis were determined in a subgroup of 21 hypocalcaemic AIDS patients. RESULTS: Mean serum calcium was 2.34 +/- 0.13 mmol L-1 in the HIV group vs. 2.46 +/- 0.10 mmol L-1 in controls ($P < 0.0001$). After adjusting for serum albumin, hypocalcaemia was present in 6.5% of the HIV group vs. 1.1% of controls. Mean serum calcium was declining according to CDC groups, and differed significantly from controls in each group. Regression coefficients of cacium vs. albumin were 0.147 amongst HIV-infected patients and 0.106 for controls. In the subgroup of hypocalcaemic patients with AIDS, 10/21 had vitamin D deficiency, six of these with low ionized calcium levels. Low serum PTH was found in 2/21 patients. Magnesium deficiency in 1/21. Of the remaining eight patients, only one had secondary hyperparathyroidism, while the other seven lacked an adequate PTH response, despite low ionized calcium levels in four subjects. CONCLUSIONS: Mean serum calcium concentrations were lower through all CDC stages, irrespective of albumin, resulting in a higher prevalence of hypocalcaemia in HIV-positive patients compared with controls. In a considerable number, this seems to be caused by vitamin D deficiency and potentially a lack of adequate PTH secretion, but further studies are needed to confirm this.

CHECK TAG(S)- Female; Human; Male; Support, Non-U.S. Gov't
MEDICAL DESCRIPTOR(S)- *Calcium --BL; *Hypocalcemia --VI; *HIV Infections --CO Acquired Immunodeficiency Syndrome --CO; Adult; Case-Control Studies ; Hypocalcemia --BL; Hypoparathyroidism --VI; HIV Infections --BL; Middle Age; Regression Analysis; Serum Albumin --ME
CAS REGISTRY/EC NUMBER(S)- *0; *7440-70-2
CAS SUBSTANCE NAME(S)- Serum Albumin; Calcium .

25. Sodium selenite and N-acetylcysteine in antiretroviral-naive HIV-1-infected patients: a randomized, controlled pilot study .
MED 98-12 98313699 NDN- 194-0099-6813-9



Look, M. P.; Rockstroh, J. K.; Rao, G. S.; Barton, S.; Lemoch, H.; Kaiser, R.; Kupfer, B.; Sudhop, T.; Spengler, U.; Sauerbruch, T.

JOURNAL NAME- Eur J Clin Invest
VOL. 28
NO. 5
1998 May
PP. 389-97
DOCUMENT TYPE- CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL
JOURNAL CODE- EN3
JOURNAL SUBSET- MEDJSM
ISSN- 0014-2972
CORPORATE AUTHOR- Department of General Internal Medicine, University of Bonn, Germany. Look@Uni-Bonn.de
PUBLICATION COUNTRY- ENGLAND
LANGUAGE- English

BACKGROUND: The aim of this work was to study the effects of combined oral administration of N-acetylcysteine (NAC) and sodium selenite (Se) on plasma glutathione (GSH), lymphocyte subpopulations and viral load in asymptomatic human immunodeficiency virus (HIV)-infected patients. METHODS: We used a prospective, randomized and controlled therapy trial with partial crossover. Twenty-four antiretroviral-naive HIV-infected outpatients at Centers for Disease Control (CDC)'93 stages I and II were randomized to receive the antioxidant combination NAC 600 mg t.i.d. and Se 500 micrograms per day for either 24 weeks (group A, n = 13) or from the end of week 12 (group B, n = 11) until the end of week 24. Thus, group B served as untreated control during the first 12 weeks. RESULTS: There was (a) a trend towards an increase in the percentage of CD4+ lymphocytes after 6 weeks (P = 0.08); (b) an increase in the CD4/CD8 ratio after 6 and 12 weeks (P = 0.02 and P = 0.04 respectively); and (c) a decrease in the absolute CD8/CD38 count and percentage of lymphocytes after 6 weeks (P = 0.002 and P = 0.033 respectively) and 12 weeks (P = 0.033, P = 0.1 respectively) in group A compared with the control period of group B. The effects observed in group A were, however, not paralleled to the same extent by group B after crossing-over to treatment after 12 weeks. In addition, erythrocyte glutathione peroxidase (GSH-Px) activity and GSH, glutathionedisulphide (GSSG) concentrations and the reduced/total GSH ratio were not affected by the treatment. Serum selenium levels increased significantly (P < 0.001) upon treatment. Viral load was not altered. CONCLUSIONS: The changes in lymphocyte subsets after NAC/Se treatment were not comparable to those after standard antiretroviral drug therapy. This, however, does not preclude per se possible benefits of antioxidant supplementation in HIV disease.

CHECK TAG(S)- Female; Human; Male

MEDICAL DESCRIPTOR(S)- *Acetylcysteine --TU; *HIV Infections --DT; *HIV-1 --DE; *Sodium Selenite --TU Administration, Oral; Adult; Erythrocytes --EN; Glutathione --BL; Glutathione Disulfide --BL; Glutathione Peroxidase --BL; HIV Infections --BL; HIV Infections --VI; Middle Age; Pilot Projects; Prospective Studies ; Reference Values; Selenium --BL; T-Lymphocyte Subsets --DE; Viral Load
CAS REGISTRY/EC NUMBER(S)- *EC-1.11.1.9; *10102-18-8; *27025-41-8; *616-91-1; *70-18-8; *7782-49-2
CAS SUBSTANCE NAME(S)- Glutathione Peroxidase; Sodium Selenite; Glutathione Disulfide; Acetylcysteine; Glutathione; Selenium .

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26. Oxidative stress and plasma antioxidant micronutrients in humans with HIV infection Ýsee comments"
MED 98-04 98103572 NDN- 194-0073-7686-5

Allard, J. P.; Aghdassi, E.; Chau, J.; Salit, I.; Walmsley, S.

JOURNAL NAME- Am J Clin Nutr
VOL. 67
NO. 1
1998 Jan
PP. 143-7
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- 3EY
JOURNAL SUBSET- MEDJSA; MEDJSM
ISSN- 0002-9165
CORPORATE AUTHOR- Department of Medicine, University of Toronto, Ontario, Canada. johane.allard@utoronto.ca
COMMENTS IN- Comment in:, Am J Clin Nutr, 1998 Aug;68(2):402-3
LAST REVISION DATE (VENDOR'S)- 981022
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

Increased lipid peroxidation induced by reactive oxygen species may play a role in the stimulation of HIV replication. In this study we compared lipid peroxidation indexes and plasma antioxidant micronutrients between 49 nonsmoking HIV-positive patients with no active opportunistic infection (25 asymptomatic and 24 with AIDS) and 15 age-matched seronegative control subjects. Breath-alkane output, plasma lipid peroxides, antioxidant vitamins, and trace elements were measured. Vitamin C (40.7 +/- 3.02 compared with 75.7 +/- 4.3 mumol/L, P < 0.005), alpha-tocopherol (22.52 +/- 1.18 compared with 26.61 +/- 2.60 mumol/L, P < 0.05), beta-carotene (0.23 +/- 0.04 compared with 0.38 +/- 0.04 mumol/L, P < 0.05), and selenium (0.37 +/- 0.05 compared with 0.85 +/- 0.09 mumol/L, P < 0.005) concentrations were significantly lower in the HIV-positive patients. Lipid peroxides (50.7 +/- 8.2 compared with 4.5 +/- 0.8 mumol/L, P < 0.005), breath pentane (9.05 +/- 1.23 compared with 6.06 +/- 0.56 pmol.kg-1.min-1, P < 0.05), and ethane output (28.1 +/- 3.41 compared with 11.42 +/- 0.55 pmol.kg-1.min-1, P < 0.05) were significantly higher in the HIV-positive

patients. These results showed an increase in oxidative stress and a weakened antioxidant defense system in HIV-positive patients. Whether supplementation of antioxidant vitamins will reduce this oxidative stress is still unknown.

CHECK TAG(S)- Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't
MEDICAL DESCRIPTOR(S)- *Antioxidants --AN; *HIV Infections --BL; *Lipid Peroxidation --PH; *Oxidative Stress --PH; *Vitamins --BL Adult; Alkanes --AN; Breath Tests; Carotenoids --BL; Cohort Studies ; HIV Infections --PP; Lipid Peroxides --BL; Middle Age; Reference Values
CAS REGISTRY/EC NUMBER(S)- *0; *0; *0; *0; *0
CAS SUBSTANCE NAME(S)- Alkanes; Antioxidants; Carotenoids; Lipid Peroxides; Vitamins .

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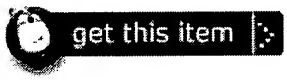
27. Serum and plasma markers of nutritional status in children infected with the human immunodeficiency virus.
MED 98-03 98068144 NDN- 194-0069-3796-0



Henderson, R. A.; Talusan, K.; Hutton, N.; Yolken, R. H.; Caballero, B.

JOURNAL NAME- J Am Diet Assoc
VOL. 97
NO. 12
1997 Dec
PP. 1377-81
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- H6F
JOURNAL SUBSET- MEDJSA; MEDJSM
ISSN- 0002-8223
CORPORATE AUTHOR- Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Md. 21287-2631, USA.
CONTRACT/GRANT NUMBER- RR-00052.RR.NCRR; U01AI2756506.AI.NIAID
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

OBJECTIVE: To determine whether reduced serum or plasma protein and micronutrient levels are common in children infected with the human immunodeficiency virus (HIV) and whether these levels are different in children with growth retardation compared to those with normal growth. SUBJECTS: Children were separated into three groups: (a) HIV-infected with growth retardation (HIV + Gr); (b) HIV-infected with normal growth (HIV+); (c) HIV-uninfected with normal growth (HIV-). All children were afebrile and free of acute infection at the time of study. During a 24-hour stay in the Pediatric Clinical Research Unit, blood was drawn for analysis of total protein, albumin, zinc , selenium , and vitamin A levels; growth measurements were obtained; and dietary intake was assessed by 24-hour weighed food intake and 24-hour dietary recall. STATISTICAL ANALYSIS: Mean differences between groups were assessed by analysis of variance, and differences in the frequency of nutrient deficiency were determined by chi 2 analysis. RESULTS: Thirty-eight children between 2 and 11 years of age were studied: 10 HIV + Gr, 18 HIV+, and 10 HIV-. No statistically

significantly differences were noted in mean levels of albumin, prealbumin, zinc , and selenium . Mean serum level of vitamin A was significantly higher in the HIV + Gr group than in the other two groups. There were no significant differences between groups in the frequency of deficiency for any nutrient studied. Mean energy and nutrient intake was similar among groups.
APPLICATIONS/CONCLUSIONS: Abnormal serum or plasma protein or micronutrient levels were uncommon in this cohort of HIV-infected children, even in children with growth retardation. Routine monitoring of the level of proteins and micronutrients studied is unnecessary in the absence of specific clinical indicators of deficiency.

CHECK TAG(S)- Comparative Study; Female; Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
MEDICAL DESCRIPTOR(S)- *Child Nutrition --PH; *HIV Infections --BL; *Micronutrients --ME; *Nutritional Status; *Serum Albumin --ME Biological Markers --BL; Body Weight; Child; Child, Preschool; Chromatography, High Pressure Liquid; CD4 Lymphocyte Count; Follow-Up Studies ; Growth Disorders --BL; Growth Disorders --CO; Growth Disorders --PP; HIV Infections --CO; HIV Infections --PP; Retrospective Studies ; Selenium --BL; Spectrophotometry, Atomic Absorption; Vitamin A --BL; Zinc --BL
CAS REGISTRY/EC NUMBER(S)- *0; *0; *11103-57-4; *7440-66-6; *7782-49-2
CAS SUBSTANCE NAME(S)- Biological Markers; Serum Albumin; Vitamin A; Zinc; Selenium

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28. The impact of high-risk patients on the results of clinical trials .
MED 98-02 98034891 NDN- 194-0067-2701-0

Ioannidis, J. P.; Lau, J.

JOURNAL NAME- J Clin Epidemiol
VOL. 50
NO. 10
1997 Oct
PP. 1089-98
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- JCE
JOURNAL SUBSET- MEDJSM
ISSN- 0895-4356
CORPORATE AUTHOR- Division of Geographic Medicine and Infectious Diseases, New England Medical Center Hospitals, Tufts University School of Medicine, Boston, Massachusetts, USA.
CONTRACT/GRANT NUMBER- T32 AI07389.AI.NIAID; R01 HS07782.HS.AHCPR
PUBLICATION COUNTRY- ENGLAND
LANGUAGE- English

The results of clinical trials may not reflect equally the experiences of all their individual participants. By modeling populations where patients have very diverse baseline risks of suffering an event of interest, it can be seen that very sick patients of high risk become the major determinants of

how many events occur in the whole population, even though they may represent only a small minority. Human immunodeficiency virus-related trials and trials of magnesium in acute myocardial infarction are analyzed. When the benefit or toxicity from a treatment varies with the baseline risk of each patient, the treatment effect may be markedly different in populations with a different representation of high- and low-risk patients. The results of small clinical trials studying heterogeneous populations with binary outcomes depend on the sampling and outcomes of very few high risk participants. Conversely, mega-trials studying homogeneous populations would miss subgroups or individuals with diverse treatment responses. In both cases, aggregate trial results may be misleading for the care of many individuals.

CHECK TAG(S)- Human; Support, U.S. Gov't, P.H.S.
MEDICAL DESCRIPTOR(S)- *HIV Infections --MO; * Magnesium --TU; *Myocardial Infarction --MO; *Randomized Controlled Trials --SN Data Interpretation, Statistical; HIV Infections --TH; Meta-Analysis; Models, Statistical; Myocardial Infarction --DT; Risk Factors
CAS REGISTRY/EC NUMBER(S)- *7439-95-4
CAS SUBSTANCE NAME(S)- Magnesium .

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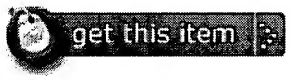
29. Serum selenium versus lymphocyte subsets and markers of disease progression and inflammatory response in human immunodeficiency virus-1 infection.
MED 97-10 97297041 NDN- 194-0047-1288-0



Look, M. P.; Rockstroh, J. K.; Rao, G. S.; Kreuzer, K. A.; Spengler, U.; Sauerbruch, T.

JOURNAL NAME- Biol Trace Elem Res
VOL. 56
NO. 1
1997 Jan
PP. 31-41
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- AU1
JOURNAL SUBSET- MEDJSM
ISSN- 0163-4984
CORPORATE AUTHOR- Department of General Internal Medicine, University of Bonn, Germany.
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

Serum selenium levels were determined cross-sectionally in 57 HIV-infected patients who were classified according to the Centers for Disease Control (CDC) 1993 classification system. Mean serum selenium levels were lower in CDC stage II (58.7 +/- 12.2 micrograms/L; $p < 0.01$; $n = 18$) and stage III (47.6 +/- 11.3 micrograms/L; $p < 0.01$; $n = 19$) HIV-infected patients, than in healthy subjects (80.6 +/- 9.6 micrograms/L; $n = 48$) and stage I patients (73.6 +/- 16.5 micrograms/L; $n = 20$). Serum selenium levels were positively correlated with CD4 count, CD4/8 ratio, hematocrit, and serum albumin ($r = 0.42$; $r = 0.39$; $r = 0.48$; and $r = 0.45$; $p < 0.01$, respectively) and inversely with

serum levels of thymidine kinase (r = -0.49; p < 0.01; n = 49) and beta 2-microglobulin (r = -0.46; p < 0.001; n = 49). In addition, serum selenium levels in 20 randomly selected AIDS-free individuals (CDC I: n = 10; CDC II: n = 10) were inversely correlated with serum concentrations of interleukin-8 (IL-8) and soluble tumor necrosis factor receptors (sTNFR) types I and II. There was no correlation with serum immuneglobulin A and total serum protein levels. The results show that the progressive deprivation of serum selenium in HIV-infection is associated with loss of CD(4+)-cells and with increased levels of markers of disease progression and inflammatory response.

CHECK TAG(S)- Female; Human; Male
MEDICAL DESCRIPTOR(S)- *CD4 Lymphocyte Count; *HIV Infections--BL; *HIV Infections--IM; *HIV-1; * Selenium --BL; * Selenium --DF beta 2-Microglobulin --ME; Adult; Biological Markers; Case-Control Studies ; CD4-CD8 Ratio; HIV Infections --ET; Inflammation --ET; Interleukin-8 --BL; Middle Age; Receptors, Tumor Necrosis Factor --ME; Thymidine Kinase --BL
CAS REGISTRY/EC NUMBER(S)- *EC-2.7.1.21; *0; *0; *0; *0; *7782-49-2
CAS SUBSTANCE NAME(S)- Thymidine Kinase; beta 2-Microglobulin; Biological Markers; Interleukin-8; Receptors, Tumor Necrosis Factor; Selenium .

---

30. Muscle involvement in human immunodeficiency virus-infected patients is associated with marked selenium deficiency.
MED 97-06 97205321 NDN- 194-0035-2060-0

Chariot, P.; Dubreuil-Lemaire, M. L.; Zhou, J. Y.; Lamia, B.; Dume, L.; Larcher, B.; Monnet, I.; Levy, Y.; Astier, A.; Gherardi, R.

JOURNAL NAME- Muscle Nerve
VOL. 20
NO. 3
1997 Mar
PP. 386-9
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- NN9
JOURNAL SUBSET- MEDJSM
ISSN- 0148-639X
CORPORATE AUTHOR- Department of Toxicology, Hopital Henri Mondor, Creteil, France.
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

NO-ABSTRACT

CHECK TAG(S)- Female; Human; Male
MEDICAL DESCRIPTOR(S)- *HIV Infections --BL; *HIV Infections --CO; *Muscular Diseases--BL; *Muscular Diseases --CO; * Selenium --DF Adult; Aged; Middle Age; Osmolar Concentration; Retrospective Studies ; Selenium --BL; Vitamin E --BL; Vitamin E --ME
CAS REGISTRY/EC NUMBER(S)- *1406-18-4; *7782-49-2

CAS SUBSTANCE NAME(S)- Vitamin E; Selenium .

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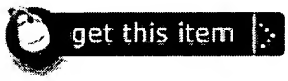
31. One-year antioxidant supplementation with beta-carotene or selenium for patients infected with human immunodeficiency virus: a pilot study .
MED 97-03 97034151 NDN- 194-0023-2193-0



Constans, J.; Delmas-Beauvieux, M. C.; Sergeant, C.; Peuchant, E.; Pellegrin, J. L.; Pellegrin, I.; Clerc, M.; Fleury, H.; Simonoff, M.; Leng, B.; Conri, C.

JOURNAL NAME- Clin Infect Dis
VOL. 23
NO. 3
1996 Sep
PP. 654-6
DOCUMENT TYPE- CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL
JOURNAL CODE- A4J
JOURNAL SUBSET- MEDJSM
ISSN- 1058-4838
CORPORATE AUTHOR- Hopital Saint-Andre, Bordeaux, France.
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

NO-ABSTRACT

CHECK TAG(S)- Human; Support, Non-U.S. Gov't
MEDICAL DESCRIPTOR(S)- *Antioxidants --TU; *Beta Carotene --TU; *HIV Seropositivity --DT; * Selenium --TU Pilot Projects
CAS REGISTRY/EC NUMBER(S)- *0; *7235-40-7; *7782-49-2
CAS SUBSTANCE NAME(S)- Antioxidants; Beta Carotene; Selenium .

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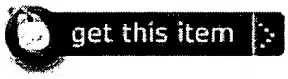
32. Effects of micronutrient intake on survival in human immunodeficiency virus type 1 infection.
MED 96-09 96245096 NDN- 194-0004-7177-7



Tang, A. M.; Graham, N. M.; Saah, A. J.

JOURNAL NAME- Am J Epidemiol
VOL. 143
NO. 12
1996 Jun 15
PP. 1244-56
DOCUMENT TYPE- JOURNAL ARTICLE; MULTICENTER STUDY
JOURNAL CODE- 3H3
JOURNAL SUBSET- MEDJSM; MEDJSX
ISSN- 0002-9262
CORPORATE AUTHOR- Department of Epidemiology, Johns Hopkins University, School of Hygiene and Public Health, Baltimore, MD, USA.
CONTRACT/GRANT NUMBER- U01-AI-35042-02.AI.NIAID; RR007222.RR.NCRR
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

The authors examined the relation between dietary and supplemental micronutrient intake and subsequent mortality among 281 human immunodeficiency type 1 (HIV-1)-infected participants at the Baltimore, Maryland/Washington, DC, site of the Multicenter Acquired Immunodeficiency Syndrome Cohort Study. Subjects completed a semiquantitative food frequency questionnaire at their baseline visit in 1984. Levels of daily micronutrient intake were examined in relation to subsequent mortality over the 8-year follow-up period by using multivariate Cox models, adjusting for age, symptoms, CD4+ count, energy intake, and treatment. The highest quartile of intake for each B-group vitamin was independently associated with improved survival: B1 (relative hazard (RH) = 0.60, 95% confidence interval (CI) 0.38-0.95), B2 (RH = 0.59, 95% CI 0.38-0.93), B6 (RH = 0.45, 95% CI 0.28-0.73), and niacin (RH = 0.57, 95% CI 0.36-0.91). In a final model, the third quartile of beta-carotene intake (RH = 0.60, 95% CI 0.37-0.98) was associated with improved survival, while increasing intakes of zinc were associated with poorer survival. Intakes of B6 supplements at more than twice the recommended dietary allowance were associated with improved survival (RH = 0.60, 95% CI 0.39-0.93), while intakes of B1 and B2 supplements at levels greater than five times the recommended dietary allowance were associated with improved survival (B1: RH = 0.61, 95% CI 0.38-0.98; B2:RH = 0.60, 95% CI 0.37-0.97). Any intake of zinc supplements, however, was associated with poorer survival (RH = 1.49, 95% CI 1.02-2.18). These data support the performance of clinical trials to assess the effects of B-group vitamin supplements on HIV-1-related survival. Further studies are needed to determine the optimal level of zinc intake in HIV-1-infected individuals.

CHECK TAG(S)- Human; Male; Support, U.S. Gov't, P.H.S.
MEDICAL DESCRIPTOR(S)- *Diet; *HIV Infections --MO; *HIV-1; *Micronutrients Adult; Cohort Studies ; Niacin --AD; Proportional Hazards Models; Questionnaires; Survival Analysis; Vitamin A --AD; Vitamin B Complex --AD; Zinc --AD
CAS REGISTRY/EC NUMBER(S)- *11103-57-4; *12001-76-2; *59-67-6; *7440-66-6
CAS SUBSTANCE NAME(S)- Vitamin A; Vitamin B Complex; Niacin; Zinc .

Citations from MEDLINE(R) DATABASE (1993 TO 1997): ME2

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33. Synoviorthesis with colloidal 32P chromic phosphate for the treatment of hemophilic

arthropathy Ýsee comments¨
MED 94-07 94201208 NDN- 193-0040-4870-0

Rivard, G. E.; Girard, M.; Belanger, R.; Jutras, M.; Guay, J. P.; Marton, D.

JOURNAL NAME- J Bone Joint Surg Am
VOL. 76
NO. 4
1994 Apr
PP. 482-8
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- HJR
JOURNAL SUBSET- MEDJSA; MEDJSM
ISSN- 0021-9355
CORPORATE AUTHOR- Department of Pediatrics, Hopital Sainte-Justine, Montreal, Quebec, Canada.
COMMENTS IN- Comment in:, J Bone Joint Surg Am, 1995 May;77(5):807-8
LAST REVISION DATE (VENDOR'S)- 950809
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

Between 1977 and 1992, we performed ninety-two synoviortheses (destruction of synovial tissue by intra-articular injection of a radioactive agent) on forty-eight patients who had a severe congenital disorder of hemostasis and chronic hemophilic synovitis that was resistant to conventional treatment. Colloidal 32P chromic phosphate was injected intra-articularly: 1.0 millicurie for knees and 0.5 millicurie for other joints. The duration of follow-up ranged from one to fifteen years. The frequency and importance of bleeding decreased in most of the patients. The range of motion of half of the joints remained stable or improved and that of the other half continued to decrease. Radiographic scores worsened progressively despite the decreased frequency of hemarthrosis. In most patients, the extra-articular leakage of the radioactive agent was slight. Chromosome breakages were observed almost exclusively in patients who were seropositive for human immunodeficiency virus and in whom the CD4-lymphocyte count was decreased from normal. The patients' level of satisfaction with the results was high.

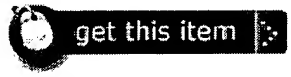
CHECK TAG(S)- Human; Male
MEDICAL DESCRIPTOR(S)- *Hemarthrosis --RT; * Phosphorus Radioisotopes --TU; *Synovial Membrane --RE Adolescence; Adult; Child; Chromium Compounds --AD; Chromosomes, Human --RE; Colloids; Injections, Intra-Articular; Joints --PH; Phosphates --AD; Phosphorus Radioisotopes --AD; Prospective Studies ; Range of Motion, Articular
CAS REGISTRY/EC NUMBER(S)- *0; *0; *0; *0; *7789-04-0
CAS SUBSTANCE NAME(S)- Chromium Compounds; Colloids; Phosphates; Phosphorus Radioisotopes; chromic phosphate .

---

34. Dietary micronutrient intake and risk of progression to acquired immunodeficiency

syndrome (AIDS) in human immunodeficiency virus type 1 (HIV-1)-infected homosexual men.

MED 94-03 94078959 NDN- 193-0029-8213-2



Tang, A. M.; Graham, N. M.; Kirby, A. J.; McCall, L. D.; Willett, W. C.; Saah, A. J.

JOURNAL NAME- Am J Epidemiol
VOL. 138
NO. 11
1993 Dec 1
PP. 937-51
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- 3H3
JOURNAL SUBSET- MEDJSM; MEDJSX
ISSN- 0002-9262
CORPORATE AUTHOR- Department of Epidemiology, Johns Hopkins University, School of Hygiene and Public Health, Baltimore, MD 21205.
CONTRACT/GRANT NUMBER- N01-AI-72634.AI.NIAID; RR007222.RR.NCRR
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

The authors sought to determine if different levels of dietary intake of micronutrients are associated with the progression of human immunodeficiency virus type 1 (HIV-1) infection to acquired immunodeficiency syndrome (AIDS). A total of 281 HIV-1 seropositive homosexual/bisexual men were seen semiannually since 1984 at the Baltimore/Washington, DC site of the Multicenter AIDS Cohort Study. Participants completed a self-administered semiquantitative food frequency questionnaire at baseline. Levels of daily micronutrient intake at baseline were examined in relation to subsequent progression to AIDS (1987 Centers for Disease Control definition; n = 108) during a median follow-up period of 6.8 years. For each nutrient, the authors used a Cox proportional hazards model to adjust for age, presence of symptoms, CD4+ lymphocyte count, energy intake, use of antiretrovirals, and use of Pneumocystis carinii pneumonia prophylaxis. The highest levels of total intake (from food and supplements) of vitamins C and B1 and niacin were associated with a significantly decreased progression rate to AIDS: vitamin C (relative hazard (RH) = 0.55, 95% confidence interval (CI) 0.34-0.91), vitamin B1 (RH = 0.60, 95% CI 0.36-0.98), and niacin (RH = 0.52, 95% CI 0.31-0.86). The relation between total vitamin A intake and progression to AIDS appeared to be U-shaped; the lowest and highest quartiles of intake did most poorly, while the middle two quartiles were associated with significantly slower progression to AIDS (RH = 0.55, 95% CI 0.35-0.88). Increased intake of zinc was monotonically and significantly associated with an increased risk of progression to AIDS (for highest vs. lowest quartiles, RH = 2.06, 95% CI 1.16-3.64). In a final multinutrient model, vitamin A, niacin, and zinc remained significantly associated with progression to AIDS, while vitamin C was only marginally significant.

CHECK TAG(S)- Human; Male; Support, U.S. Gov't, P.H.S.
MEDICAL DESCRIPTOR(S)- *Acquired Immunodeficiency Syndrome --EP; *Bisexuality; *CD4-Positive T-Lymphocytes; *Homosexuality; *HIV Seropositivity --CO; *HIV-1; *Nutritional Status; *Trace Elements --AD; *Vitamins --AD Acquired Immunodeficiency Syndrome --ET; Adult; Antiviral Agents --TU; Baltimore --EP; Confidence Intervals; District of Columbia --EP;

Energy Metabolism; Follow-Up Studies ; HIV Seropositivity --BL; HIV Seropositivity --DT; HIV Seropositivity --ME; Leukocyte Count; Nutrition Surveys; Proportional Hazards Models; Risk Factors; Survival Analysis
CAS REGISTRY/EC NUMBER(S)- *0; *0; *0
CAS SUBSTANCE NAME(S)- Antiviral Agents; Trace Elements; Vitamins .

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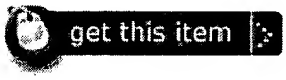
35. Molecular modeling studies suggest that zinc ions inhibit HIV-1 protease by binding at catalytic aspartates.
MED 94-01 94008892 NDN- 193-0016-6822-3



York, D. M.; Darden, T. A.; Pedersen, L. G.; Anderson, M. W.

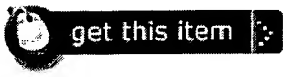
JOURNAL NAME- Environ Health Perspect
VOL. 101
NO. 3
1993 Aug
PP. 246-50
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- EI0
JOURNAL SUBSET- MEDJSM
ISSN- 0091-6765
CORPORATE AUTHOR- Laboratory of Molecular Toxicology, National Institute of Environment Health Sciences, Research Triangle Park, NC 27709.
CONTRACT/GRANT NUMBER- HL27995.HL.NHLBI
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

Human immunodeficiency virus type 1 protease is inhibited in vitro by zinc ions at neutral pH. The binding site of these ions is not known; however, experimental data suggest that binding may occur in the active site. To examine the possibility of zinc binding in the active site, molecular dynamics simulations in the presence and absence of zinc have been carried out to 200 psec. The results are compared with the 2.8-A crystallographic structures of a synthetic HIV-1 protease, and a zinc binding site at the catalytic aspartate residues (Asp-25, Asp-25') is proposed. Molecular dynamics simulations show that the zinc ion remains stably bound in this region, coordinating the carboxylate side chains of both aspartate residues. Interaction with zinc does not disrupt the dimeric structure of the protein or significantly alter the structure of the active site. These data are consistent with experimental studies of HIV-1 protease inhibition by zinc and give strong evidence that this is the binding site that leads to inactivation.

CHECK TAG(S)- Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
MEDICAL DESCRIPTOR(S)- *Aspartic Acid --ME; *HIV Protease Inhibitors --ME; *Models, Biological; *Models, Chemical; * Zinc --ME Binding Sites
CAS REGISTRY/EC NUMBER(S)- *0; *56-84-8; *7440-66-6
CAS SUBSTANCE NAME(S)- HIV Protease Inhibitors; Aspartic Acid; Zinc .

36. Role of nutritional status and weight loss in HIV seroconversion among Rwandan women.

MED 93-08 93267397 NDN- 193-0006-9908-0



Moore, P. S.; Allen, S.; Sowell, A. L.; Van de Perre, P.; Huff, D. L.; Serufilira, A.; Nsengumuremyi, F.; Hulley, S. B.

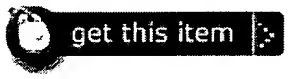
JOURNAL NAME- J Acquir Immune Defic Syndr
VOL. 6
NO. 6
1993 Jun
PP. 611-6
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- JOF
JOURNAL SUBSET- MEDJSM
ISSN- 0894-9255
CORPORATE AUTHOR- Department of Medicine, University of California, San Francisco.
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

To investigate nutritional status and heterosexual human immunodeficiency virus (HIV) transmission, we performed a nested case-control study of sexually active, adult women in Kigali, Rwanda. Forty-five women who seroconverted during the 24-month study period were compared to 74 women who remained seronegative throughout the study. Seroconvertors and nonseroconvertors did not differ in preseroconversion serum levels of vitamin A, carotenoids, vitamin E, selenium , albumin, ferritin, or cholesterol. Weight loss, however, was a significant predictor of eventual HIV seroconversion. Subsequent seroconvertors lost an average of 1.5 kg during the first 6 months of the study compared with a 1.0-kg gain ($p = 0.001$) for nonconvertors. Nine of 27 (33%) seroconvertors, compared with one of 44 (2%) controls, lost at least 5 kg in the 6-month period beginning 1 year before their seroconversion (odds ratio, 21.5, 95% confidence interval 4.1-112). The association between weight loss and seroconversion was independent of other potential risk factors such as socioeconomic status, pregnancy, and genital ulcer disease. In addition to these findings for measured weight loss during follow-up, reported weight loss before enrollment was also a risk factor for subsequent seroconversion. Additional studies of heterosexual HIV transmission are needed to determine whether or not weight loss is causally related to susceptibility for HIV infection.

CHECK TAG(S)- Female; Human
MEDICAL DESCRIPTOR(S)- *HIV Seropositivity --IM; *Nutritional Status Adolescence; Adult; Case-Control Studies ; Enzyme-Linked Immunosorbent Assay; HIV Antibodies --IM; HIV Infections --TM; HIV Seropositivity --EP; HIV Seropositivity --TM; HIV-1 --IM; Risk Factors; Rwanda; Sex Behavior; Weight Loss
CAS REGISTRY/EC NUMBER(S)- *0
CAS SUBSTANCE NAME(S)- HIV Antibodies .

Citations from MEDLINE(R) DATABASE (1990 TO 1993): ME3

37. Nutritional status of HIV-infected patients during the early disease stages.
MED 90-12 90375776 NDN- 192-0099-0708-6



McCorkindale, C.; Dybevik, K.; Coulston, A. M.; Sucher, K. P.

JOURNAL NAME- J Am Diet Assoc
VOL. 90
NO. 9
1990 Sep
PP. 1236-41
DOCUMENT TYPE- CLINICAL TRIAL; JOURNAL ARTICLE; RANDOMIZED CONTROLLED TRIAL
JOURNAL CODE- H6F
JOURNAL SUBSET- MEDJSA; MEDJSM
ISSN- 0002-8223
CORPORATE AUTHOR- San Francisco General Hospital, California 94110.
CONTRACT/GRANT NUMBER- M01-RR00070.RR.NCRR; AI-27666.AI.NIAID
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

Nutritional status was monitored in two groups of patients infected with human immunodeficiency virus (HIV) for up to 16 months. Twenty-six subjects were recruited from patients enrolled in acquired immunodeficiency syndrome treatment protocols in the early stages of the disease. Body weight, percent body fat, serum albumin, total protein concentration, hemoglobin, hematocrit, and total lymphocyte count were monitored monthly. Four-day food intake records were kept every 4 months. In the 19 patients followed for 16 months (Group 1), a significant (p less than .05) decrease was observed in body weight, percent body fat, body mass index (BMI), and total protein concentration. Seven subjects (Group 2), with more advanced disease than Group 1, demonstrated a significant (p less than .05) decrease in total lymphocyte count over a 5-month period. This latter group fell just below the normal range for hemoglobin and hematocrit concentrations during the study period. With the exception of a decrease in vitamin B-6, zinc , and total energy intake, food records closely matched the Recommended Dietary Allowance for the age group. Thus, we conclude that decreases in body weight, percent body fat, and BMI may be the earliest indication of decreased nutritional status in HIV-infected patients.

CHECK TAG(S)- Human; Male; Support, U.S. Gov't, P.H.S.
MEDICAL DESCRIPTOR(S)- *Acquired Immunodeficiency Syndrome --ME; *Diet; *Nutritional Status Acquired Immunodeficiency Syndrome --BL; Acquired Immunodeficiency Syndrome--DT; Adult; Double-Blind Method; Energy Intake; Hematocrit; Hemoglobins; Middle Age; Nutritional Requirements; Randomized Controlled Trials ; Zalcitabine --TU; Zidovudine --TU
CAS REGISTRY/EC NUMBER(S)- *30516-87-1; *7481-89-2

CAS SUBSTANCE NAME(S)- Zidovudine; Zalcitabine .

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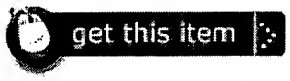
38. Relationship of serum copper and zinc levels to HIV-1 seropositivity and progression to AIDS.
MED 91-12 91366578 NDN- 192-0042-7146-3



Graham, N. M.; Sorensen, D.; Odaka, N.; Brookmeyer, R.; Chan, D.; Willett, W. C.; Morris, J. S.; Saah, A. J.

JOURNAL NAME- J Acquir Immune Defic Syndr
VOL. 4
NO. 10
1991
PP. 976-80
DOCUMENT TYPE- JOURNAL ARTICLE
JOURNAL CODE- JOF
JOURNAL SUBSET- MEDJSM
ISSN- 0894-9255
CORPORATE AUTHOR- Department of Nutrition, Johns Hopkins Hospital, Baltimore, Maryland.
CONTRACT/GRANT NUMBER- N01-A1-72634; RR007222.RR.NCRR
PUBLICATION COUNTRY- UNITED STATES
LANGUAGE- English

Dietary, serum, and tissue levels of copper and zinc were determined at baseline in a cohort of homosexual men to investigate the relationship of these factors to human immunodeficiency virus type 1 (HIV-1) seropositivity and subsequent progression to AIDS. Using a nested case control design, 54 asymptomatic HIV-1 seropositives who later progressed to AIDS were compared with 54 HIV-1 seropositives who did not progress and 54 seronegatives (mean follow-up time 2.5 years). Serum levels of copper and zinc were estimated from frozen serum samples, tissue levels from stored toenail samples, and dietary intakes from a semiquantitative food frequency questionnaire administered at baseline. Neither dietary copper and zinc nor their levels in toenails were associated with HIV-1 seropositivity or progression to AIDS. However, serum copper levels were higher ($p = 0.002$) in HIV-1-seropositive progressors (mean = 115.6 micrograms/dl; SD = 17.1) than the seropositive nonprogressors (mean = 109.0 micrograms/dl; SD = 15.8) and the seronegatives (mean = 101.9 micrograms/dl; SD = 16.7). Conversely, serum zinc levels were lower ($p = 0.016$) in the seropositive progressors (mean = 85.2 micrograms/dl; SD = 11.5) than the seropositive nonprogressors (mean = 90.7 micrograms/dl; SD = 12.0) and the seronegatives (mean = 92.0 micrograms/dl; SD = 14.7). Furthermore, in a logistic regression, higher serum copper (odds ratio per 20-micrograms/dl increase = 2.23; 95% confidence interval = 1.02-4.87) and lower serum zinc (odds ratio per 20-micrograms/dl increase = 0.30; 95% confidence interval = 0.14-0.66) predicted progression to AIDS independently of baseline CD4+ lymphocyte level, age, and calorie-adjusted dietary intakes of both nutrients.(ABSTRACT TRUNCATED AT 250 WORDS)

CHECK TAG(S)- Human; Male; Support, Non-U.S. Gov't; Support, U.S. Gov't, P.H.S.
MEDICAL DESCRIPTOR(S)- *Acquired Immunodeficiency Syndrome --BL; *Copper --BL; *HIV Seropositivity --BL; * Zinc --BL Acquired Immunodeficiency Syndrome --DI; Acquired Immunodeficiency Syndrome --EP; Adult; Biological Markers; Cohort Studies ; Copper --AN; Diet; HIV Seropositivity --DI; HIV Seropositivity --EP; Multicenter Studies ; Nails --CH; Prospective Studies ; Risk Factors; Toes; United States --EP; Zinc --AN
CAS REGISTRY/EC NUMBER(S)- *0; *7440-50-8; *7440-66-6
CAS SUBSTANCE NAME(S)- Biological Markers; Copper; Zinc

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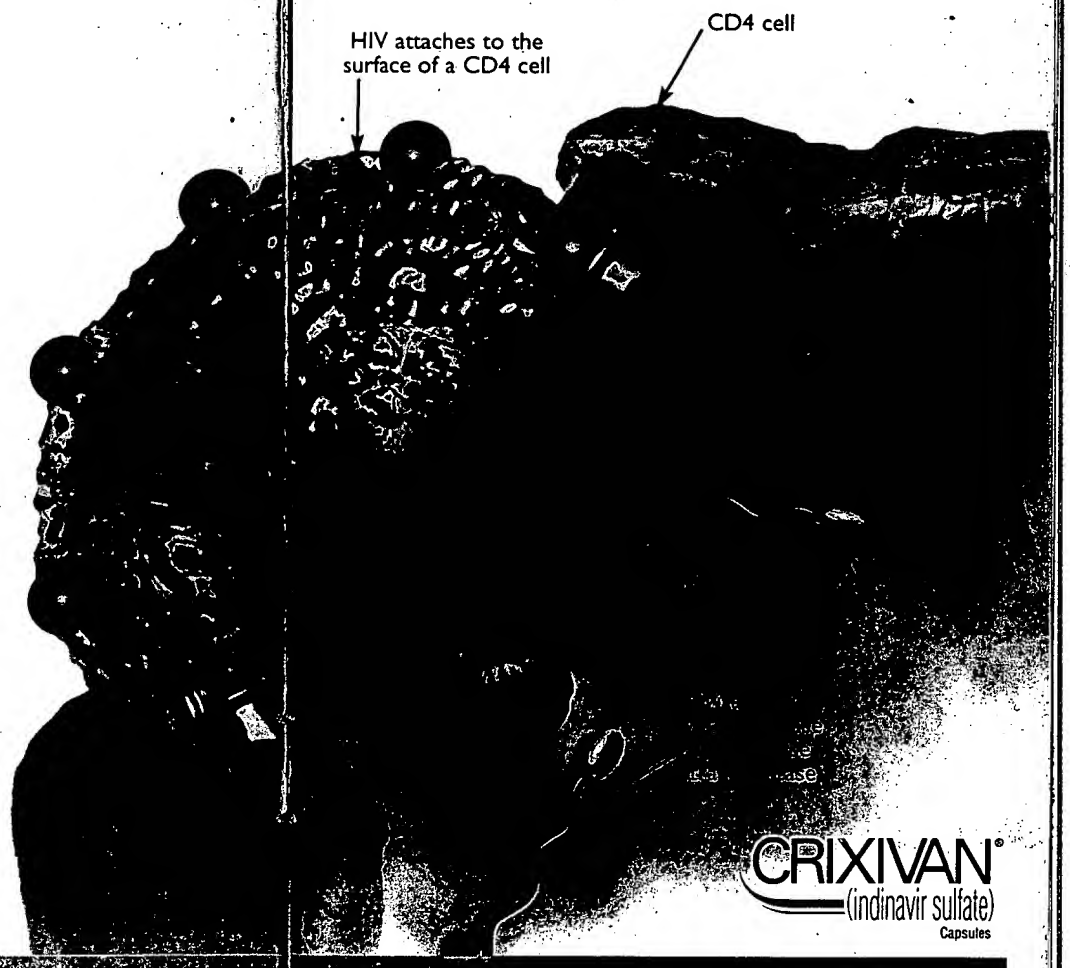
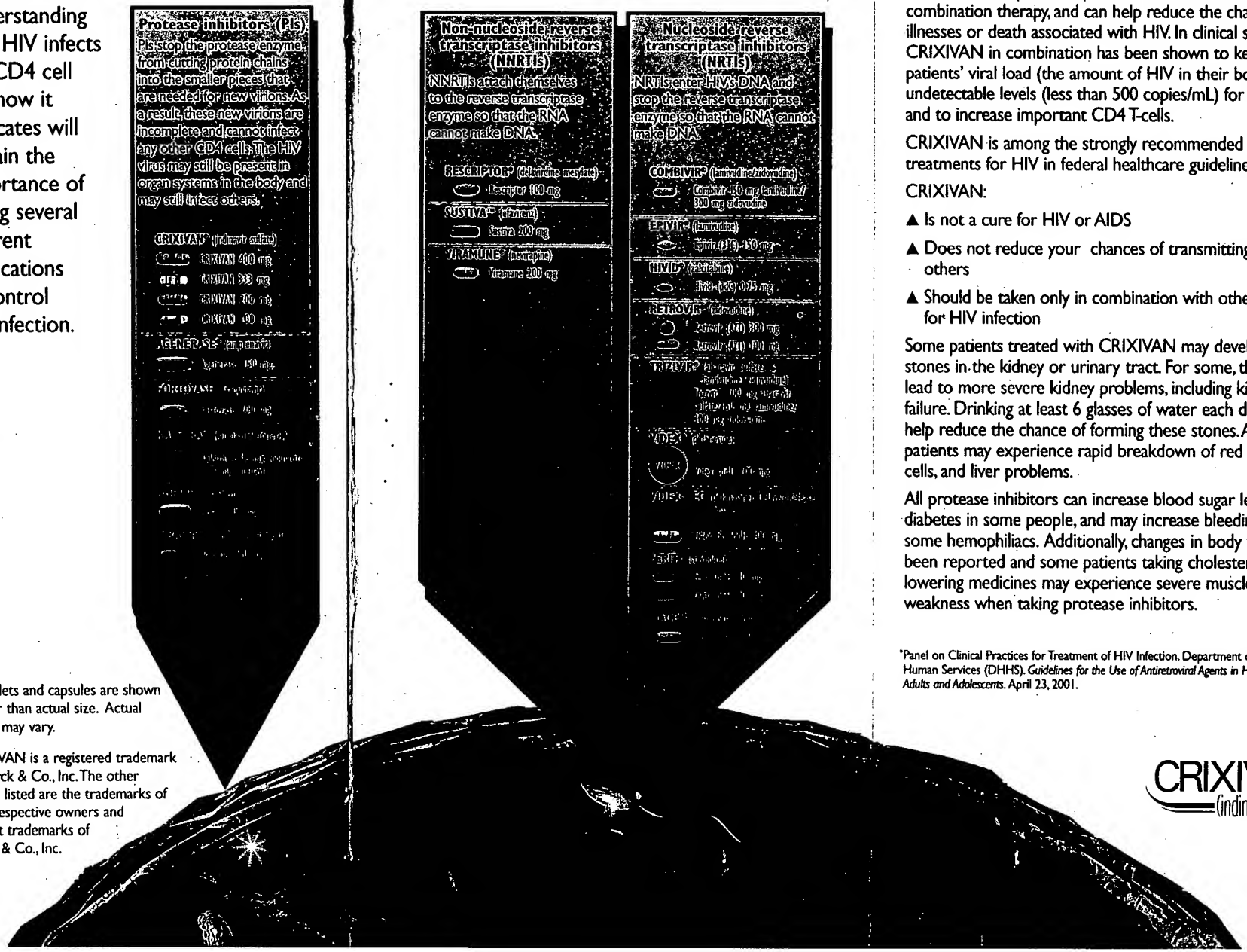
While the viral RNA carries instructions for producing more viruses, it must first undergo the next stages in the life cycle before replication can occur.



Understanding how HIV infects the CD4 cell and how it replicates will explain the importance of taking several different medications to control the infection.



All tablets and capsules are shown smaller than actual size. Actual colors may vary.

Things you should know about CRIXIVAN

CRIXIVAN is a powerful protease inhibitor used in combination therapy, and can help reduce the chance illnesses or death associated with HIV. In clinical studi CRIXIVAN in combination has been shown to keep patients' viral load (the amount of HIV in their bodie undetectable levels (less than 500 copies/mL) for one and to increase important CD4 T-cells.

CRIXIVAN is among the strongly recommended treatments for HIV in federal healthcare guidelines.*

CRIXIVAN:

- ▲ Is not a cure for HIV or AIDS
- ▲ Does not reduce your chances of transmitting HI others
- ▲ Should be taken only in combination with other dr for HIV infection

Some patients treated with CRIXIVAN may develop stones in the kidney or urinary tract. For some, this c lead to more severe kidney problems, including kidne failure. Drinking at least 6 glasses of water each day n help reduce the chance of forming these stones. Also, patients may experience rapid breakdown of red bloc cells, and liver problems.

All protease inhibitors can increase blood sugar level diabetes in some people, and may increase bleeding f some hemophiliacs. Additionally, changes in body fat h been reported and some patients taking cholesterol-lowering medicines may experience severe muscle pa weakness when taking protease inhibitors.

*Panel on Clinical Practices for Treatment of HIV Infection. Department of He Human Services (DHHS). *Guidelines for the Use of Antiretroviral Agents in HIV-Infe Adults and Adolescents.* April 23, 2001.

CRIXIVA (indinavir

Additional things you should know about CRIXIVAN

ALERT: Find out about medicines that should not be taken with CRIXIVAN. There are some common medications and AIDS-related medications you should not take with CRIXIVAN.

Additionally, severe muscle pain and weakness have occurred in patients also taking cholesterol-lowering medicines called "statins." Also, taking CRIXIVAN with any products containing St. John's wort, an herbal supplement, is not recommended because it may lead to increased viral load and possible resistance to CRIXIVAN. Discuss all medications you are taking or plan to take with your doctor.

Before you take VIAGRA (sildenafil) with CRIXIVAN, talk to your doctor about possible drug interactions and side effects. If you take VIAGRA and CRIXIVAN together, you may be at increased risk of side effects of VIAGRA, such as low blood pressure, visual changes, and penile erection lasting more than 4 hours. If an erection lasts longer than 4 hours, you should seek immediate medical assistance to avoid permanent damage to your penis. Your doctor can explain these symptoms to you.

You can take CRIXIVAN on an empty stomach, or with a light snack. It's important to take all of your medication according to your prescribed schedule. With CRIXIVAN and other HIV medicines, it is important NOT to skip a dose, take an extra dose, or take a "drug holiday."

For more detailed information about CRIXIVAN, please read the Patient Product Information in the pocket of this booklet. Also enclosed is a copy of the physician Prescribing Information.

CRIXIVAN®
(indinavir sulfate)
Capsules